Hepatoprotective Properties of Herbal Plants: A Review

SAGAR SINGH JOUGH[1], RAJESH GOUR,[2] AKHLESH KUMAR SINGHAI[3]
[1]*Research Scholar, School of Pharmacy, LNCT University, Bhopal, Madhya Pradesh, India*
[2]*Associate Professor, School of Pharmacy, LNCT University, Bhopal, Madhya Pradesh, India*
[3]*Director, School of Pharmacy, LNCT University, Bhopal, Madhya Pradesh, India.*

Abstract*— The body's many physiological functions depend on the liver, which is the most significant organ in this regard. The presence of inflammatory cells in the liver's tissue distinguishes hepatitis, an inflammation of the organ. kinds A, B, C, D, and E relate to the five basic kinds of viruses. The weight of disease and mortality is particularly concerning for these five categories. A serious health issue that affects the pharmaceutical business, drug regulatory organisations, and health care providers is liver damage or malfunction. For a very long time, liver illness has been treated using herbal medications. The body's immune system is the organ that makes diagnoses the infection by activating immune system cells, chemokines, and cytokines, as well as releasing an inflammatory mediator, in order to show an instant reaction. The immune system is strengthened and modulated by them. Polysaccharides, proteins, flavanoids, lignans, and other phytoconstituents originating from plants sustain liver disorders and boost the immune system. Numerous herbs that have been reported to be immunomodulatory and hepatoprotective. The goal of the current review is to gather information on potential phytochemicals found in hepatoprotective and immunomodulatory plants.

Index Terms- Hepatoprotective herb, immunomodulatory herb, nitric oxide

I. INTRODUCTION

Medicinal plants existing even before human being made their appearance on the earth. Medicinal plants, in India have been collected from the wild and cultivated for millennia. The Rig-Veda, written in India between 4800 and 1600 BC, is the earliest recorded in India for the use of trees, shrubs, herbs and grass combination in curing ailments[1]. According to WHO, 80% of the world population uses plant-based remedies as their primary form of healthcare. Throughout the human history people have relied on natural products and plants in a particular, to promote and maintain good health and to fight sickness, pain and disease[2]. The use of herbal medicines is evidence to approach for the treatment and prevention of disease is known as phytotherapy flourishing the quest for significant source of synthetic and herbal drugs[3].

Nowadays herbal products are symbol of safety as when compare to the synthetic products they are unsafe to human life and environment. Now the era of natural products started with the hope of safety and security. Over three-quarter ofpeople in the world depend upon plant extracts to maintain their good health. Of the 2, 50,000 higher plant species on the earth, more than 80,000 are of medicinal values. Indian biodiversity centers contains over 45,000 different plants species, of these, about 15,000 – 20,000 plants have good medicinal value. Among those only 7000 – 7500 plant species are used for their medicinal properties by traditional communities.

In India, Ayurveda, Siddha, Unani and Folk (tribal) medicines are the major system of indigenous medicines since ancient time. Among those Ayurveda describes 700 species, Unani 700 species, Siddha 600 species, Amchi 600 species and Modern Medicine around 30 species. The *Rigveda* (5000 BC) has described 67 medicinal plants, *Yajurveda* 81 species, *Atharvaveda* (4500-2500 BC) 290 species, *Charaka Samhita* (700 BC) and *Sushruta Samhita* (200 BC) had described 1100 and 1270 species respectively, in compounding of drugs, these are still used in the classical formulations.[4]

About liver, functions and diseases

Liver is the largest glandular organ in the body contributing about 1/50th of the total body weight, which regulates various important metabolic functions and performs many other

functions. Liver is also known by a Greek word "*Hepato".* It lies in the upper right quarter of the abdominal cavity. It is reddish- brown in colour and divided into four lobes of unequal sizes and shape.[5] The lobes of the liver are made-up of small lobules, just visible to the naked eye. The lobules are hexagonal from outside and are formed by cubical shaped cells which are hepatocytes and are arranged in pairs of columns radiating from central vein. The sinusoids (blood vessels with an incomplete walls) containing a mixture of blood from the very small branches of the portal vein and hepatic artery. Their arrangement allows the arterial blood and venous blood (with a high concentration of nutrients) to mix and come into close contact with liver cells. The posterior surface of the liver is called portal hepatic, where various structures enter and leave the gland (Figure.1 and Figure. 2). The portal vein enters carrying blood from the stomach, spleen, pancreas and the small and large intestines. The hepatic artery enters, carrying arterial blood, is a branch from the celiac artery, which is a branch from the abdominal aorta. The right and left hepatic ducts leave, carrying bile form the liver to the gall bladder[6].

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Functions of the liver[7,8]

Liver cells called as hepatocytes are responsible for many functions that are pivotal to normal functioning of human body and they can be basically divided into 3 categories.

a. Regulation, synthesis and secretion.
b. Storage.
c. Purification, transformation and clearance.

a. Regulation, Synthesis and Secretion:

Hepatocytes are helpful for the regulation, synthesis and secretion of many substances important in maintaining the body's normal state.

- Hepatocytes are metabolically active cells those uptake glucose, mineralsand vitamins from portal and systemic blood and store them.
- Hepatocytes can produce blood clotting factors, I, II, V, VII, IX, XI,antithrombin, transporter proteins, cholesterol and bile components.
- Regulating blood levels of cholesterol and glucose.
- In the first trimester, fetus in pregnancy, the liver is the main site for RBCproduction.

b. Storage:

The liver is designed to store important substances such as glucose (in the form of glycogen), fat-soluble vitamins (vitamin A, D, E, and K), folate, vitamin B12 and minerals, such as copper and iron.

c. Purification, Transformation and Clearance:

The liver plays a major role in removal of waste products, biotransformation of drugs and toxins to less harmful compounds in the blood.

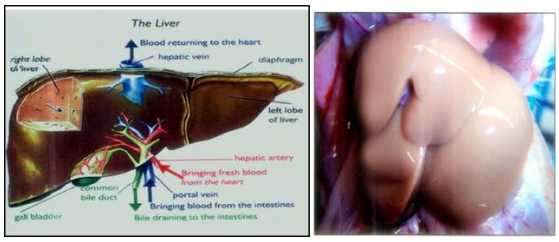

Fig 1. The Liver

Fig 2. Isolated Rat Liver

Liver diseases and toxicity of liver[9,10,11]

Liver toxicity is mainly caused by certain chemicals and organiccompounds having certain structures. Haloalkanes, certain antibiotics, chemotherapeutics, CCl_4 peroxidised oil, chlorinated hydrocarbons, aflatoxin etc., excess consumption of alcohol, infections and autoimmune disorders are a few among the reasons for liver damage. The liver is unique in its function processing the chemicals and drugs, which enters the blood stream. Many of these chemicals are difficult for the kidney to excrete out of the body. The liver helps by removing these chemical from the blood stream and changing them into products that can be readily removed through bile or urine. In this processes, unstable toxic products are sometimes produced and cause injury to liver.

Acute Liver Injury: Acute liver failure develops in a short period as a consequence of viral hepatitis, drug-induced (e.g. paracetamol overdose), chemical-induced (e.g. carbon-tetrachloride) or alcohol-induced toxicity, or dueto rejection after liver transplantation.

Chronic Liver Injury: Chronic cholestasis or long-term exposure to alcohol, drugs or chemicals can result in liver failure progressing into liver fibrosis. Liver fibrosis is characterized by deposition of scar tissue and its end-stage is calledliver cirrhosis. Other causes of chronic liver failure are viral hepatitis, metabolic diseases like Wilson disease (copper storage disease) or auto-immune diseases (e.g. primary biliary cirrhosis, primary sclerosing cholangitis). During chronic liver injury, the endothelial cells, hepatocytes and cholangiocytes can be damaged due to the accumulation of toxic metabolites, reactive oxygen species and bile acids. This results in the activation of Kupffer cells and the recruitment of inflammatory cells and the subsequent release of growth factors (e.g. Transforming Growth Factor-β (TGF-β), cytokines, reactive oxygen species that induce the activation and proliferation of hepatic stellate cells. These cells are major players in the development of liver fibrosis. A major consequence is a remodelling of the ECM that leads to deposition of scar tissue (fibrosis) and liver dysfunction[16]. Therefore, the activation and proliferation of stellate cells are considered key events in liver fibrosis.

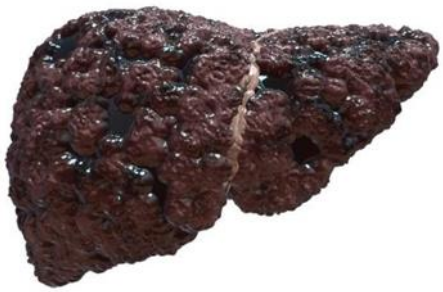

Fig 3. Chronic Liver Disease

HEPATOTOXIC AGENTS[17-19]

These generally promote the healing process of the liver.

In India, The use of herbal products for the management of disease has a long history, starting with Ayurvedic management, and proceeding to the European and Chinese alternative systems of ancient medicines. Medicinal plants are significant sources of hepatoprotective drugs. According to one estimate, more than 700 mono- and polyherbal preparations in the form of decoction, tincture, and tablets have been used in various liver disorders. The 21st century has seen a paradigm shift toward therapeutic evaluation of herbal products in liver disease models by carefully synergizing the strengths of the traditional system of medicine with that of the modern concept of evidence-based therapeutical screening, authentification, and randomized placebo-controlled clinical trials to support clinical efficacy. A large number of plants and formulations have been claimed to show hepatoprotective activities. Around 160 active constituents from 101 plants are claimed to have post

liver protecting activity. In India, quite eighty seven plants square measure used in 33 patented propitiatory multi-ingredient plant formulations. In spite of the tremendous advances made, no important and safe hepatoprotective agents are obtainable in modern medicine Therefore, due importance has been given globally to develop primarily plant-based hepatoprotective medications that are effective against a range of liver disorders. A drug having helpful results on the liver is understood as a hepatoprotective drug. On the other hand, drugs having toxic effects on the liver are called hepatotoxic drugs. Clinical analysi has conjointly shown that herbals have real utility in the treatment of diseases. In the last 30 years, severa hepatotoxins have been used commonly in d-galactosamine, carbon tetrachloride, acetaminophen, and thioacetamide, and more recently Concanavalin A (ConA) and lipopolysaccharide (LPS) has been developed. ConA and LPS do not reflect the clinical pattern of human disease, which indicates a grea advantage in the study of cellular mechanisms involved in autoimmune liver disease. The galactosamine model is a highly selective hepatotoxi that causes liver damage similar to human viral hepatitis via depletion of uridine nucleotides, which subsequently diminishes the synthesis of RNA an proteins. Galactosamine intoxication in rats disrupts the membrane permeability of the plasma membrane, causing leakage of the enzymes form the cell, whic leads to the elevation of serum enzymes. Hence, a significant rise in the transaminase levels could b taken as an index of liver damage. Galactosamine has great liver specificity compared to other toxic groups, such as paracetamol, acetaminophen, and carbo tetrachloride because hepatocytes have high levels of galactokinase and galactose-1-uridyltranseferase, and galactosamine does not affect other organs. Galactosamine induces hepatotoxicity with spotty hepatocytes, necrosis, and marked portal and parenchymal infiltration. Galactosaimine also induce the depletion of uridine diphosphate (UDP) by increasing the production of UDP-sugar derivates, which causes inhibition of RNA and protein synthesis, leading to cell membrane deterioration. The current study is aimed toward assembling information-supported reported works on promising phytochemical from herbal plants that are tested in hepatoxicity models. The review deals with fact-finding work done on herbals helpful in the treatment of liver ailments.

The failure of the synthetic drugs in the treatment of hepatic diseases and the search for potent immunomodulatory agents are leading us to the world of herbal medicine in search of a product in nature for use in the protection and cure of dreaded liver diseases. Till date, there is only one protective natural drug; that, too, is not curative and also has its limitations in protecting the liver from viral attacks. The list of herbal hepatoprotective agents has been summarized in Table 1.

S.No	Plant Name	Category	Name of Active Constituent	Mechanism
1.	*Allium sativum*	Organosulfur compounds	Organosulfur compounds	Prevention of GSH depletion, alteration of GSH-dependent enzymes
2.	*Buddleja officinalis*	Phenyl ethanoid	Acetoside	Decreased levels of AST, ALP
3.	*Camellia sinensis*	Polyphenols	Catechin	Inhibited hepatocellular apoptosis
4.	*Cistus laurifolius*	Flavanoid	Quercetin	MDA, AST level decreased.
5.	*Eglets viscose*	Flavanoid	Ternatin	Decreased lipid peroxidation
6.	*Gingko biloba*	Polyphenols	Polyprenols	ALT, AST, ALP level decreased
7.	*Hibiscus sabdariffa*	Polyphenols	Protocatechuic acid	LDH,AST, ALP Level decreased
8.	*Magnolia indica*	Triterpine	Lupeol	Decreased Level of SGOT,SGPT
9.	*Nigella sativa*	Quinones	Thymoquinonone	Scavenger of superoxide, hydroxyradical, and singlet molecular oxygen.
10.	*Ocimum basilicum*	Phenolic Acid	Rosmarinic acid	AST, ALP, SGOT level decreased.

Table 1:- List of herbal hepatoprotective agents

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