IJAPC

INTERNATIONAL JOURNAL OF AYURVEDA AND PHARMACEUTICAL CHEMISTRY

Greentree Group Publishers

Int J Ayu Pharm Chem

REVIEW ARTICLE

www.ijapc.com

e-ISSN 2350-0204

Liver Disorders and Potential Medicinal plants: A Review Study

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ABSTRACT

Liver is a large organ that maintains metabolic functions and detoxification processes in the body. Liver disease occurs throughout the world irrespective of age, sex, region or race. According to World Health Organization, about 46% of global diseases and 59% of the mortality is because of chronic diseases and almost 35 million people in the world die of chronic liver diseases. Liver and its dysfunctions are highly defined and well described in Ayurveda in relation to pathogens (*dosha*), tissues (*dhatu*) and its development. Liver disorders include a group of diseases of the liver and biliary system.

There are no any complete, safe and effective remedies available for liver disorders. Treatments used are found to give only symptomatic relief. A number of herbs, classical and significant formulations in various dosage forms are mentioned in *Ayurved* classics for liver diseases.

The details of experimental and pre-clinical studies conducted on single and compound Ayurvedic preparations for their efficacy against liver cancer and other hepatic ailments are also important. They strongly emphasize Ayurvedic products as a scientifically feasible medical practice and an unconventional entity. But well planned clinical trials to establish the safety and efficacy is the need. Ayurvedic medicine has an opportunity to develop new drugs and contribute as safe and cost effective treatment for Liver disorders. In this paper, authors have reviewed all the liver disorders and potential medicinal plants which are scientifically proved.

KEYWORDS

Liver disorders, treatment modalities, synergetic action, Herbal products

Greentree Group Publishers

Received 20/05/18 Accepted 16/06/18 Published 10/07/18

INTRODUCTION

The liver is a large and an essential organ connected with physiological processes, metabolic functions and detoxification. Bile production, absorbing and metabolizing bilirubin, fat, proteins and carbohydrates, supporting blood clots, vitamin and mineral storage, blood filtration, synthesis of angiotensinogen are the major functions of liver. It is site for various diseases process[1].

Throughout the world, liver disorders arise irrespective of age, region, and sex. According to World Health Organization, 35 million people in the world die due to chronic disease[2]. Liver diseases have been ranked as the fifth mainly general cause of death as per national statistics in the UK[3]. It is tenth most common cause of death in India, [as per W.H.O.] and may affect every one in five Indians. Every year around 10 lakh patients of liver cirrhosis are newly diagnosed. It is the 14th foremost cause of deaths in the world. It could be the 12th leading cause of deaths in the world by 2020[4].

Data published by WHO in May 2014, in India 216,865 or 2.44% of total deaths are due to liver diseases. India is ranked 61 in the world[5]. The main causes of liver disorders are viruses, excessive drug therapy, pollution and alcoholic intoxication. The treatment of chronic liver disease depends on the cause. Antiviral, corticosteroids, interferon, bile acids etc[6] drugs are used as per the diseased conditions.

Conventional medicines used in the management of liver diseases are often too expensive, have limited efficacy, and difficult to tolerate or sometimes efficacy may develop serious adverse effects[7]. Medicinal plants and Ayurved formulations are in demand due to their natural and therapeutic activities, safe and cost effective[8].

The development of innovative therapeutic approaches; plant drugs and formulations of traditional systems could offer an opportunity to treat the various liver diseases and gives new hope for the future. More than 120 scientific research and review articles/papers are available on liver diseases/ liver disorders. Two review articles on Indigenous drugs for liver and hepatoprotective *Ayurvedic* plants based on plant drugs gave idea about role of indigenous drugs as hepatoprotective drugs[9, 10]. In this paper, authors have reviewed all the liver disorders and therapeutic modalities through herbal drugs.

METHODOLOGY

For the present review, A literature search was conducted for various liver disorders and medicinal plants used for liver disorders from Ayurved classical texts, PubMed and Google Scholar. Various scientific research and review articles published from 2001 to 2017 were identified through PubMed and Google scholar websites using MeSH terms. The search included the following keywords: medicinal plants, formulations, liver diseases, hepatoprotective, hepatic disorders.

LIVER - AYURVED AND MODERN PERSPECTIVE

Ayurved view

Ayurveda is based on **maintaining the health of healthy people and cure the diseases of sick people.** In the ancient literature *Jyotisthana, Kalakhanda, Raktadhara, Raktashaya, Takima, Yakna, Yakritkhanda, Yakritpinda* terminologies are used for liver. *Yat* means (conversion) and *krit* (to do) [11].

Liver and its dysfunctions are highly defined and well described in *Ayurveda* classics in relation to *dosha, dhatu* (tissues) and *srotas* (channel). The liver may be affected in the diseases involving, *rakta* and *mansa dhatu (*blood and muscle), *Hrid* (heart), *pranavaha srotas* (respiration) and *mala* (excretion) systems. Significance of liver in the context of blood as an important constituent of human biology is specific to all the system of medicine. Spleen is an organ that controls the quality of circulating red blood cells by removing & destroying all worn out red cells and helps fight infections by producing some of the antibodies, phagocytes and lymphocytes.

Raktavah srotas, Ranjak Pitta and liver

Raktvaha srotas is the channels associated with the formation, transportation and transformation of *rakta dhatu* directly or indirectly. *Yakrita* [Liver] and *Pleeha* [Spleen] are considered as main organs of *Raktavaha srotas*[12].

During embryonic development origin of *Yakrit* and *Pleeha* takes place from *Shonit* (blood) [13] and after birth for a particular time period production of blood takes place in *Yakrit* and *Pleeha.*

In early foetal age blood is produced by the liver and spleen which explains the close association between blood and the liver since foetal life. Ayurveda refers the cells in the blood as blood (*rakta dhatu)* and the fluid in the blood [the plasma] is included in body fluids (*rasa dhatu*).

Liver and spleen is the location of *Ranjaka pitta*. It is subtype of *pitta* most closely related to the liver. The word *ranjaka* means, to give color. It gives color to the

blood and to all tissues throughout the body (it even influences skin, hair, and eye color). The function of *Ranjaka pitta* is the disintegration of haemoglobin and produces bile and liver enzymes and governs the transformation of *rasa dhatu* (plasma) into *rakta dhatu* (red blood cells). Due to functional integrity between liver, spleen, stomach and bone marrow, if anyone is affected other will also get affected[14].

Modern view

The liver has a major role in the maintenance of equilibrium in intermediate metabolism of carbohydrates, regulation of fatty acid, triglyceride and cholesterol metabolism, amino acid and ammonia metabolism, protein synthesis, degradation and glycoproteins, drugs metabolism, drugs degradation and metabolism of porphyrins, bilirubin. It converts sugar into glycogen, carbohydrates and proteins into fats, toxic ammonia into nontoxic urea, etc. It produces bile, blood coagulating and anti-coagulating factors, proteins and enzymes. It stores critical trace elements and vitamins and is responsible for detoxification and elimination of various toxins, carcinogens, nitrogen-containing waste products and alcohol[15].

Due to Pollution toxins, modified life style, excessive consumption of alcohol and therapeutic drugs use often exploits the metabolic function of the liver. This leads to various liver disorders [hepatitis, cirrhosis, alcoholic liver disease] and eventually produces Liver cancers or tumours.

LIVER DISORDERS ACCORDING TO AYURVED

Liver/biliary system/liver disorders are described in Ayurved literature in different contexts. It includes *Pandu [anaemia], Kamala, Kumbha kamala, Halimaka [Jaundices and its types], Jalodara (Ascites), Yakritdalhadara (hepatomegaly), Yakritpliha dara, Yakrit kshaya (cirrhosis of liver), Pittasmari (cholithiasis)* etc [16]. The liver may be affected in the diseases involving, *rakta* and *mansa dhatu* (muscle and blood), *hrid* (heart), *pranavaha srotas* (respiration) and mala (excretion) systems.

General *samprapti* [etio-pathology] of liver disorders-

Due to foresaid *nidana* (etiology), all the three *dosha* get aggravated. *Agnimandhay* (impaired digestive power) is considered the basic etiological factor in any diseases. Due to aggravated *dosha, agnimandhya* and *ajirna* (Indigestion) the accumulation of abnormal toxic fluids creates blockage in the channels (*srotorodh*) which inhibits the bile secretion resulting in the

enlargement of liver and other Liver diseases[17].

Liver/ Spleen is directly or indirectly involved in the following diseases.

Pandu- *Panduta* means pallor; it is the most common characteristic feature of all the varieties of *Panduroga* in which reduction in the count of erythrocytes is seen. All three *dosha* are vitiated in but mainly *Pitta* plays dominating role in which *rasa dhatu* and *rakta dhatu* are mainly affected. Due to *pitta* provoking etiology, aggravation of *Pitta* and destruction of *rakta dhatu* (haemolysis) lead to *Panduta*[18].

Kamala- *Pandu* and *Kamala* are said to be the diseases which are interrelated. *Kamala* is classified under *pitta* (biliary) diseases; *ranjaka pitta* (type of biliary fluid) is the main cause in the pathogenesis[19]. The liver secretes *Pachaka pitta*, stored in the *pittashaya* (gall bladder), gets reabsorbed and leaves a portion of original bile (*tyakta drava pitta*). Concentred bile when circulated, it becomes critical and any derangement diminished digestive and metabolic activity (*agni vaishamya*) [20].

Excess break down of erythrocytes results in to *Koshthashrita kamala [Bahupitta kamala]* which increases the production of *Pitta*, while obstruction in *Pittavaha srotas* (intra hepatic cholestasis) results for *Shakhashrita kamala*.

Kumbha Kamala- Halimak, Alasa- When jaundice continues for more than one month and symptoms become serious with dark yellow colored urine, faeces, deep yellow colored eyes, swelling of the body, joints pain, is become ***Kumbha-Kamala***, when it develops fever, pain in the limbs, vertigo, physical indolence, drowsiness and thinness known as ***Lagharaka***. Excessive preponderance of the deranged *Vata* and *Pitta* is known as *Alasa*, otherwise known as ***Halimaka***[21, 22].

Gulma- It is palatable, hard to touch and round in shape mass, a lump between *hṛdaya* and *basti* [gastrointestinal tract] either moving or stationary; undergoing increase or decrease and round in shape is described as *Gulma*. The aggravated *Vata* takes away either *Kapha, Vata* or *Rakta* from their place and forms a mass or growth in gastrointestinal tract especially in those parts of tract which are lying under epigastrium to hypogastrium and obstruct the channel of intestine, causing pain in the region of epigastrium [*hrit*], umbilicus[*nabhi*], hypogatrium [*basti*] and in the flanks[both *pashwa*][23].

Udarroga- Yakrutodara and Pleehodara - The morbid *doshas* which have accumulated in the body vitiate and block

the *srotas* (channels) related to conduction and transportation of *sweda* (sweat) and *ambu* (water) and cause 8 types of *Udara roga* (abdominal disorders) by further contaminating *Prana Vayu*, *Agni* (metabolic fire) and *Apana Vayu*[24]. *Yakrutodara* and *Pleehodara* are the types of eight *Udarroga*. In both, enlargements of spleen and liver is seen along with accumulation of fluid in abdomen, anorexia, retention of urine and faces, thirst, reddish tings over abdomen.

Agni (digestive power) is the basic cause to develop *samprapti* (pathogenesis). *Atisanchita* (Excess accumulation) of *kapha dosha*, intake of *Abhishyandi* (*kapha* producing substances) and *Vidahi* (excessive burning) foods in excessive quantity are said to aggravate *Kapha*, *pitta* and *Rakta.* The accumulation of abnormal toxic fluids around the liver creates blockage (*srotorodh*). This block in the body's transport system leading to pathological increase of Pitta and resulting in liver and spleen enlargement (*Yakrutodara* and *Pleehodara)*[25, 26].

Jalodara- Immediately after *panchakarma* procedures if water is consumed or due to administration of excess fats, oil, ghee etc through treatments then *udakavaha srotas* (channels carrying or transporting water in the body) is affected. As a result, fluid accumulates in the *udara* (abdominal cavity) and causes a disease called *Jalodara* (ascites)[27].

Madatyaya –Due to excessive and the improper use of alcohol caused '*Madatyaya*'. It is *Tridoshaja Vyadhi* (disease caused by involvement of all three *Doshas* - *Vata, Pitta and Kapha*)[28, 29]. It is also characterized by excessive accumulation of morbid *dosha* in the body. The disease *Madatyaya* is classified into *Vatika*, *Paittika*, *Kaphaja*, *Sannipataja* – based on *Doshic* predominance. *Madatyaya* is not just an alcohol intoxication, dependence or withdrawal state, but it is the condition where multiple systemic dysfunctions are involved with immediate and acute manifestations to chronic and severe manifestations. Neurological, gastro-hepatic and cardio-pulmonary manifestations are the commonest features seen in the patients of *Madatyaya* which is also similar to the descriptions of alcoholism.

Granthi/ Arbud specific to Yakrit/ Spleen- *Granthi*, [minor neoplasm] is a localized small swelling within the subcutaneous fat tissue, muscle or blood veins; it is round, erect, and knotted.

Arbuda [major neoplasm] is a spherical, stable, massive, painless swelling occurring at one site; it expands slowly with deeper roots.

On the basis of *tridosha* concept, *pitta* present in each and every cell is responsible for digestion and metabolic function. In liver cancer, the decreased state of deranged metabolism (*dhatwagni* imbalance) results in the excessive growth of the liver tissue and creates metabolic crisis where anabolic phase exceeds the catabolic phase (aggravation of *vata* forces and suppression of *kapha* forces) resulting in proliferation. It is clearly stated that liver enlargement (*ekadesavriddhi*) is accompanied by weight loss (*anyasthaniya kshaya*) in *Yakrut*/*Pleeha Granthi* or *Arbud* (liver cancer) [30].

TYPES OF LIVER DISEASES – MODERN PERSPECTIVE[31]

According to different causes the different types of liver diseases are largely classified.

Viral Hepatitis [common type] - Due to viral infection, liver becomes inflamed. A number of viruses can cause liver inflammation but it is mainly due to the hepatitis viruses. These viruses are of different strains and referred to as A, B, C, D and E. Transformation of diseases may occur due to blood, blood product or sexual intercourse.

Parasitic Liver Infections-Parasites can infest the liver and damage it over time. Blood flukes or liver flukes are the reason and often acquired from sheep or cattle livestock and sometimes from other organisms like snails. It enters in the human body by consuming of contaminated water or food.

Alcoholic Hepatitis - It is where the liver becomes inflamed and damaged due to excessive alcohol consumption usually over a long period of time. It is known as type of toxic hepatitis.

Toxic hepatitis is where the liver becomes inflamed and damaged from exposure to a number of different chemicals such as nutritional, herbal supplements, OTC drugs, cleaning chemicals, pesticides etc.

Alcoholic Liver Diseases (ALD) - Alcoholic abuse is responsible for more than 55% of deaths and the prevalence of ALD is closely correlated with per capita alcohol consumption. ALD is structural and functional liver damage by long term alcohol consumption. Its major threat to alcoholics causing morbidity and mortality but not seen in all alcoholics (50%). In alcoholics, factors as genetics, viral liver disease, poor nutrition, hepatotoxin exposure increase risk of ALD[32]. Abnormal retention of lipids within a cell, damage in liver, cirrhosis and development of HCC may be seen.

Only 35% of patients with substantial alcohol abuse develop advanced stages of liver disease. It suggests that many other factors like gender, obesity, drinking

patterns, dietary factors, non-sex-linked genetic factors, and smoking involves developing pathophysiology of ALD[33]. 90–100% heavy and long-term drinkers develop fatty liver but only 10–35% develops alcoholic hepatitis and 8–20% develops alcoholic cirrhosis.

Types of alcohol-related liver disease

Fatty liver disease- It is the abnormal accumulation of fat in liver cells. It is considered as pre-stage of alcohol-related liver disorders.

Non-alcoholic fatty liver disease (NAFLD) - In India prevalence of this disease is 9-32 % with higher prevalence in those with overweight or obesity, diabetes or pre-diabetes and accumulation of fat in the liver [34]. In India, it may be cause of cirrhosis and hepatocellular carcinoma (HCC) [35].

Alcoholic hepatitis- It is inflammation of the liver caused by drinking alcohol. In mild type Liver impairment, while in severe type serious complications such as failure or death may occur.

Alcoholic cirrhosis- It is the most serious type of alcohol-related liver disease. Symptoms of alcoholic liver cirrhosis are similar to other alcohol-related liver disorders include jaundice, portal hypertension, skin itching (pruritus).

Cirrhosis- The etiology of the liver cirrhosis is due to the diffused degeneration and infiltration of parenchyma that results in the structural alteration of fat lobules, dense perilobular connective tissue formation, and development of regeneration areas. It is a complication of liver disease that involves loss of liver cells and irreversible scarring of the liver[36].

Hepatic Coma- When neurologic symptoms associated with severe liver disease it is known as hepatic coma. An elevation of the blood ammonia results from the breakdown of nitrogenous products in the bowel which reaches the brain in toxic quantities as the result of portal venous collateral circulation around the liver and/or as the result of defective liver function. Symptoms like jaundice, hepatomegaly, splenomegaly, and ascites are seen.[37]

Liver Cancer- Liver cell cancer (hepatocellular carcinoma) and carcinoma of the biliary epithelium (cholangio carcinoma) are very common. Fibrolamellar carcinoma, squamous cell carcinoma, epithelial hemangioendothelioma, angiosarcoma, Kaposi's sarcoma, hepatoblastoma, and hepatocellular adenoma are also seen. Metastatic involvement of the liver is also very common due to spreading of cancer from other parts of the body [38].

Hepatocellular carcinoma (HCC) - Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver. Approximately 7.5 million new patients worldwide and 22000 in India are diagnosed with HCC each year[39]. It is the fifth most frequent neoplasm and ranks third on the list of most lethal cancers. About 80% of all HCC occurring in India are attributable to chronic liver damage such as cirrhosis or hepatitis. The other risk factors include alcohol consumption, obesity, nonalcoholic fatty liver disease, exposure to carcinogens, such as aflatoxins and nitrosamines[40]. Inflammation leads to fibrosis and cirrhosis and regenerating nodules progress toward a neoplastic lesion and contribute to HCC development.

Hepatotoxicity- Various drugs produce toxicity and are responsible for asymptomatic increase of enzymes, injury and liver failure. Condition of liver transplantation and viability of life occurs due to reactions of nearly 75% of the idiosyncratic drug[41].

COMPARISON OF AYURVED LIVER DISORDERS WITH MODERN TERMINOLOGY [Table 1]

Table 1 Comparison -Ayurved term of Liver disorders with nearer to Modern terminology

Ayurved terms	Modern terms
Gulma	Abdominal Tumor
Udarroga	Abdominal Disorders
Yakritodara	Hepatomegaly [Enlargement of Liver]
Pleehodara	Splenomegaly [Enlargement Of The Spleen]
Jalodara	Ascites
Pandu	Anaemia
Kamla	Jaundice
Koshthashrit Kamla	Haemolytic Jaundice
Shakhashrit Kamla	Hepatic Jaundice
Kumbhakamla	Chronic Non-obstructive Jaundice with Oedema
Halimak, Alasa	Chronic Obstructive Jaundice
Madatyaya	Alcoholism
Granthi	Neoplasm- Minor
Arbuda	Neoplasm- Major,
Yakridvidradhi	Abscess of Liver
Plihavidradhi	Abscess of Spleen

There is no any clear description and diagnosis of Cirrhosis and Hepatic coma available in Ayurved, but both can be resembled an advanced stage of kumbha kamala.

CURRENT MANAGEMENT OF LIVER DISEASES

There are no any complete, safe and effective remedies available for Liver dysfunction. Medicinal products used are found to give only symptomatic relief to patient with hepatic disorder without managing the fundamental cause to the symptoms.

Treatment according to Modern science-

Various specialized treatments are utilized in various liver disorders. Supportive treatments are needed in hepatitis to prevent from infections and preserve hydration. It may need a long-term medical care to control and minimize the consequences of hepatic disorders. In Cirrhosis and critical stages of various liver disorders, drugs should be used that control the protein absorption from the diet. In cirrhosis of liver when the detoxification process disturbed and increased blood ammonia levels may create hepatic encephalopathy (lethargy, confusion, and coma). Low sodium diet and diuretics may be required to minimize water retention.

In ascites removal of ascites fluid (fluid accumulated in the abdominal cavity), operations may be required to treat portal hypertension and minimize the risk of bleeding. Liver transplantation is the final option for patients whose livers have failed[42].

Ayurved management [43, 44, 45] – Liver diseases when treated in traditional ways the drug toxicity appears to be less as compared to modern medicine. The principle of management of liver diseases differs in Ayurveda, from western modern medicine. The basic treatment adopted for the liver diseases comprise of the pacification of *Pitta dosha* and purification of *rakta dosha*. The treatment of *Yakrit Rogas* (Liver diseases) includes drugs having *pitta* pacifying, *shothhara* [anti-inflammatory], *anulomana* [mild purgative], and *deepana-pachana* [appetizer, digestive] actions which may help in normalizing the *agni* and level of *pitta* in the body. Secondly, drugs with bitter test predominance have *Rakta-shodhak* properties [Blood Purifier], having *sheeta* [cold] in nature help in controlling the vitiated *pitta dosha*.

AYURVEDA HERBS/ PRODUCTS FOR LIVER DISEASES

India has well-recorded and well-practiced knowledge of folklore and traditional system of medicine. More than hundreds of preparations which contains medicinal plants and minerals and metals are used in ASU [*Ayurved, Siddha, and Unani*] system for the treatment of various liver disorders. Nearly 70% people rely on ASU system for liver diseases. Until date, there are enormous medicinal plants, which are used extensively in many diseases in different parts of India. Knowledge about the drugs used in liver disorders and having hepatoprotective activity is probably the best gift traditional health care system has offered to the current society.

More than 600 marketed herbal formulations are sold all over the globe having hepatoprotective activity. Around 170 phytoconstituents are isolated from various medicinal plants have been assessed for hepatoprotective activity. In India, more than 90 medicinal plants are used in different combinations in the preparations of herbal formulations[46].

A number of herbs and classical and significant formulations in various dosage forms are mentioned in *Ayurved* classics for liver diseases. The basic approach is to formulate various compounds to select several herbs with properties that address key aspect of the individual case, such as involvement of *dosha*, *prakriti*, digestive power, symptoms, tissue, organs and channels involved. Single herb can have many properties; herbs can choose to address more than one particular element of the overall treatment. Research has proven the efficacy of several medicinal plants and herbo-mineral formulations prescribed in Ayurved in the treatment of liver disease[47]

Scientifically proven anticancer activity of Plant drugs

Amalaki [Emblica officinalis] - *Rasayan karma* of *Amalaki* acts at various levels improve the essential seven vital tissues and establish physical strength and protect the body against deleterious effect of radiotherapy & chemotherapy.

Research has proven that *Amalaki* is preventing/ameliorating the toxic effects of hepatotoxic agents, impart beneficial effects on liver function and mitigate hyperlipidemia and metabolic syndrome. Animal experiments suggest protective effects of *Amalaki* against chemical-induced hepatocarcinogenesis. The free radical scavenging, antioxidant, anti-inflammatory activities and modulation of the xenobiotic detoxification process and lipid metabolism has proven the hepatoprotective actions of *Emblica* [48].

Arjuna [Terminalia arjuna] - It is a diuretic and a general tonic for liver cirrhosis. It protects the DNA from any possible damage from toxins. It accelerates clotting and thereby promotes quick healing of the wound. It is used for the purposes of cardio protection. It appears to reduce pressure and pulse rate[49]. The aqueous extract of *Terminalia arjuna* protects liver and kidney tissues against oxidative damages and used as an effective protector against CCl_4 induced hepatic and renal damages probably by increasing antioxidative defence activities[50].

Agnimukh [Semecarpus anacardium Linn] – It is *rasayana* [rejuvenates] and useful in *vata* disorders. It augments the appetite, improves digestion, eliminates

waste toxins and clears up *srotasas* – the micro channels of all the systems, hence facilitates the nourishment of all the tissues (*dhatus*).

It decreases bilirubin and abnormal nucleic acid content; normalizes cancer marker activities, lysozomal enzymes, glycoprotein content, immunosuppression, and hyperlipidemia; reduces alpha-fetoprotein to normal range and regulates abnormal mineral metabolism; cures hypoglycemia by activating gluconeogenic enzymes, thereby increasing the synthesis of glucose; controls abnormal lipid peroxidation and maintains antioxidant defence status of the host, prevents tumor initiation by the metabolic activation of carcinogens; replaces necrotic tissues by newly regenerated hepatocytes[51,52].

Bhrungaraj [Eclipta alba] **-** It acts as hepatoprotective and stimulates regeneration hepatic cells, increases bile production, enhances digestion, stimulates breaking down and expelling toxins and improves overall liver health. It reduces inflammation, exerts antihepatotoxic effects, and improves liver enzymes. The flavonoid content (Wedelolactone) appears to be related to its hepatoprotective action[53, 54]. It significantly reduces elevated liver enzymes, level of alanine transaminase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP).

Bhumi amalaki [Phyllanthus niruri] **–** It is act on *ranjaka pitta*, treats viral hepatitis, chronic hepatitis and it acts as a cholagogue. It is also useful for clearing and preventing gallstones. Due to phyllanthin and hypophyllanthin it acts hepatoprotective against drugs or toxins. It suggests the suppressive effect on HBsAg secretion and HBsAg mRNA expression and the inhibition of hepatitis B virus olymerase activity[55].

Bhunimba [Swertia chirayita] **-** It is useful for several liver disorders like hepatitis, hepato-toxic disorder, fatty liver, hepato cellular carcinoma. Extract of *chirayta* significantly inhabited cell proliferation and tissue adopsis[56, 57].

Daruharidra [Berberis aristata] **-** Due to astringent and hepato protective it is used in hepatitis and liver disorders. *Daruharidra* is improving the regeneration and functional recovery of beta cells; showing suppressing action on hepatic drug metabolizing enzymes; it blocking the carcinogenesis process[58].

Guduchi [Tinospora cordifolia] **–**It is a well-known tonic and rejuvenator, while simultaneously being a powerful blood and liver cleanser, as being useful in conditions of hepatitis and jaundice due to its ability to detoxify the liver. In a trial, liver

toxicity was induced in rats, followed by the administration of an alcohol extract of *Guduchi*. The extract protected the livers of the rats, showing that *guduchi* has significant hepatoprotective properties[59]. *Guduchi* was found to have anti-tumour properties. *Tinospora* alcoholic extract was exposed to activate tumour-associated macrophages (white blood cells that eat cancer cells) [60].

Haritaki [Terminalia chebula]- It is considered as rejuvenate and an eliminator of toxins and wastes from throughout the body, improving digestion and promoting healthy weight loss. It provides beneficial effects to colon, liver, spleen and lungs. The active compounds of *Terminalia chebula* increase the activities of antioxidant enzymes which in turn obviously protect liver for oxidative damage. Lower levels of serum AST and ALT in TCP-PCT and PCP-TCT rats suggest that *Terminalia chebula* extract provides protection against paracetamol induced liver injury due to its free radical scavenging[61].

Kalmedha [Andrographis paniculata]- Current study proved that andrographolide reduced concanavalin A-induced liver injury and inhibited hepatocyte apoptosis. It has been reported to be efficacious in chronic hepatitis B viral infection. Extract of *Kalmedha* repairs the hepatic injury and/or restore the cellular permeability, and reducing the toxic effect of liver toxicity by preventing enzymes leakage into the blood circulation [62, 63].

Kalaunj [Nigella sativa] **-** It is reported that *N. sativa* (0.2 mL/kg) intra peritoneally relieves the deleterious effects of ischemia reperfusion injury on liver[64], protects hepatic tissue from deleterious effects of toxic metals[65].

Kasani [Cichorium intybus] – It stimulates the flow of bile into the duodenum (cholagogues) or stimulate the production of bile by the liver (choleretic), stomachic, deobstruent used in the treatment of almost all kinds of liver disorders like sluggish liver, enlargement of spleen, biliary stasis (stoppage of bile) & jaundice. The extract of *Kasni* leaves relieves pain & inflammation both when applied on affected area. Due to antioxidant and hepatoprotective activity it suppresses the oxidative degradation of DNA in tissue debris[66].

Katuki [Picrorrhiza kurroa]- *Kutaki* is bitter in taste, cooling and removal of excessive fire energy from the body, best of removal of excessive *Pitta* from the body via colon. *Katuki* helps in restoration of Liver functions by overcoming fatty liver changes.

Research on animal studies suggested *Picrorrhiza kurroa* effective in hepatitis B

infection and promising effect on bilirubin, SGOT, SGPT, preventing liver toxicity and improves hepatic glycogen preservation. It also promotes liver regenerating activities by restoring cytochrome [67, 68]

Kumari [Aloe vera]- *Kumari* is digestive stimulant, mainly release of bile from the liver and improving liver functions. Extracted *A. vera* polysaccharides (AVGP) exerts a potent protective effect against chronic alcohol-induced liver injury. It acts as hepatoprotective along with Antioxidant, lipolysis, anti- inflammatory activities[69].

Pippali [Piper longum] – Due to bioavailability enhancing effects; potential hepato-protective activity of Piperine increases the absorption of many drugs and nutrients from the gastrointestinal tract by various mechanisms. It alters the membrane dynamics and increases permeability at site of absorption[70] and has great therapeutic potential in treatment of liver ailments[71].

Punarnava [Boerhaavia diffusa]- *Punanrnava* is *shothghna* [anti-inflammatory] and *mootral* [diuretic] because of its large quantity of nitrate contents. In cirrhosis and ascites it improves liver condition, rejuvenates, and detoxifies liver and skin. It has been shown to be hepatoprotective and choleretic, cardiokine, anti-cancer and anti-oxidant.

Due to its hepato-protective action, increase in normal bile flow in rats and significant decrease in serum bilirubin levels suggest strong choleritic activity, strong stimulating action on the secretory activity of liver[72, 73].

Sharapunkha [Tephrosia purpurea] -It is diuretic, tonic and laxative, removes obstructions, stimulate the flow of bile; used in enlargement and obstruction of liver. It protects the liver against ccl4 induced oxidative damage probably by increasing antioxidative defence activities[74].

Madhuyashti- Glycyrrhiza glabra- The root is used as a drug for strengthening muscle and bone, increasing physical strength and treating peptic ulcers. It can help in nonalcoholic fatty liver disease. It reduces elevated liver enzymes.

The active component glyccyrrhizic acid, saponin and triterpene play an important role in arresting production of inflammatory cytokine, reduce the hepatotoxicity and protect the Liver[75].

Scientifically proven Ayurved Liver products

A number of classical, proprietary, patented and significant formulations in the various dosage forms are mentioned in Ayurved for liver diseases. In dealing with

problems of the liver, the primary goal in Ayurveda is to enhance liver detoxification processes and help protect against further damage.

Over all more than 125 products are used in various disorders such as jaundice, liver and spleen disorders. Classical or proprietary Ayurved liver products are the combination of the above mentioned plant drugs along with minerals and metals. It was observed that maximum formulations having *Daruharidra*, *Sharpunkha*, *Rohitak*, *Kalmedh*, *Bhumi Amalaki*, *Katuki* and *Nimba* as main content are used frequently.

More than 24 clinical papers and 92 experimental studies have been shown the efficacy of highest selling Ayurveda product Liv 52, on liver disorders. Research suggested its noteworthy effect as preventive and curative on the viral hepatitis, prophylaxis of adverse effect of chemotherapy in tuberculosis, liver cirrhosis, and alcoholic hepatitis etc[76, 77].

An experimental study of *Arogyavardhini vati* has proven the protective effect against CCl_4 induced hepatotoxicity in rats[78, 79], it has proven anti-oxidant properties. Clinically *Arogyavardhini vati* proven in clearing of HBSAg and normalise Liver Transminase in Hepatitis B.[80].

Innovative, oral, US patented, plant-based proprietary extraction method product *Periban*[81] is detoxifier and useful in non-alcoholic Fatty Liver disease (NASH) with Anti-aging and anti-oxidant properties. Scientific evidence of efficacy and long term safety in pre- clinical and clinical studies is proven in various models.

Periban product is an example of extraction method for concentrating pharmacologically active fractions of plants. It provides a synergistically active compound containing approximately 5%-25% extract of *Andrographis paniculata*, 10%-30% extract of *Boerhavia diffusa*, 25%-50% extract of *Phyllanthus niruri*, and 15%-40% extract of *Tephrosia purpurea*. The synergistically active compound provides greater therapeutic benefit than the individual ingredients alone, or the combined ingredients in different concentration ranges[81].

21 cases of Hepatitis were treated with an Ayurvedic drug *L 2002* in the dose of two tablets (500 mg each), twice a day. Out of these 21 cases, 10 were negative for Hbs Ag (Group A) and 11 were positive for Hbs Ag (Group B). The most significant effect was found in the patients of hepatitis B, where 9 out of 11 patients became HbsAg negative (with the kit method). The promising results in hepatitis B necessitate

a double blind, controlled, long-term evaluation of *L 2002*[82].

An open study on 10 patients manifesting symptoms of alcoholic hepatitis was conducted to test the safety and efficacy of the herbal hepato protective drug *Hepafyte*. The drug was well tolerated and except for mild rise in tri glyceride in one patient no adverse effect was noted. This study paves the way for further double blind trials[83].

45 cases of surgery related hepato-biliary disorders [7 with history of cholecystectomy, 21 operated for other gall bladder pathology, 12 with hepatitis and 5 with T-tube biliary drainage after cholecystectomy] were treated with an Ayurvedic drug *L 2002*. Study suggests a positive role; Ayurvedic drugs can play in surgery related hepatic dysfunctions[84].

DISCUSSION

According to Ayurved the disease process inevitably leads to conjugation of *dosha and dushya*, to conquer a disease therefore, separation of *dosha and dushya* is the main aim of the treatment. During the disease process metabolism of affected tissues is disturbed, it produces toxic-waste material [*Ama*] which accumulates in the body. This accumulated waste is responsible for continuation of disease process, therefore treatment of *ama* through appetizer and digestives [*Dipan , pachan*] drugs is necessary. The drugs having actions like laxative (*rechana*), diuretics (*mutrala*), pacifying *vata* and *Kapha,* carminative, digestion of *ama* qualities are used for various types of liver diseases. The general approach of the various pharmacological activities of various dugs are to increase power of all *agni* [*Jatharagni*, *Dhatwagni*, *Bhutagni*], digest the waste toxin [*ama*] (eliminating toxins) and reduce the size of wound by scraping [*lekahana*], Drastic [*Bhedan*] and *Chhedan* action.

Ayurved formulations are created as a single drug or mixture of more than two drugs. Traditional therapeutic herbal formulations/combinations recognize the possible synergistic and counter balancing effects of herbs and achieves therapeutic efficacy. No disease has just one single symptom. So there is a need of different medicines (plants) to treat the various signs and symptoms of a disease. Due to synergism the various plants in a polyherbal medicine may increase the effectiveness and potency of the formulation, reduce unwanted effects, make the formulation more palatable, and increase life span. Best combination of poly-herbal combination provides higher activity against a disease. It provides efficacy which may not be present in single plant. It also eliminates the need of

taking more single drugs at a time for ease of patients.

Multiple types of active constitutes present in formulations act against a disease/complication. Different constituents cure a disease by different mechanism hence provides a complete therapy. Sometimes active constitutes present in the plants are not enough to attain the necessary therapeutic efficacy[85].

Medicinal plant drugs used in various formulations of liver diseases are having Anti-viral, Hepatoprotective, Anti hepatotoxic, Anti-Cholestasis, Hypochloremic effects, Anti-microbial, Antioxidant, Anti-inflammatory, Immunomodulatory actions.

Combination of various drugs existing in the formulations is having hepatoprotective activity and they restore the functional efficiency of the liver by protecting the hepatic parenchyma and promoting hepatocellular regeneration. It facilitates the rapid elimination of acetaldehyde and ensures protection from alcohol-induced hepatic damage; reduces the lipotropic effect in chronic alcoholism and prevents fatty infiltration of the liver. In pre-cirrhotic conditions, plant arrests the progress of cirrhosis and prevents further liver damage[66]. Mineral and herbomineral preparations are used in various types of Liver disorders. The study showed that *Shilajit* exhibited cytotoxic effects and inhibited the carcinogenic potential of cyclophosphamide. In experimental studies, it has also been observed that *Shilajit* activates macrophage and enhances cytokinerelease. The antioxidant and restorative effects of *swarna bhasma* in rats have been demonstrated[77].

Several pharmaceutical preparations containing either known Hepatoprotective or other plants are claimed to provide significant hepatoprotection in CCl_4 damage. It is debatable whether the use of multiple plants in one formulation will provide synergistic effect or have different plants or same plants with different names in verifying dosages. There is need to undertake studies for understanding the effects of these plants and to identify their role in different hepatic disorders. The based is in vitro testing animal models of liver injury and clinical trials focused on a group of patients with a common allopathic diagnosis. While designing these experiments, there is a need to take into account the Ayurvedic approaches to pathogenesis and treatment based on Ayurved principles[9].

CONCLUSION

Increase in no. of patients with liver disorders needs safe and cost effective

treatment. Various treatment modalities are available but outcomes are still considered underprivileged. Herbal medicine has become a major contributor for liver diseases. The increasing numbers of various researches are being undertaken on various herbal medicines and formulations show a positive sign on the future of drug development.

Due to its culturally accepted nature, comparatively fewer side-effects, and the compatibility with the human body, herbal medicines are now increasing in demand for various Liver disorders, not only in the developing world, but also in developed western countries.

Research works carried out on various models at preclinical and clinical studies of single as well as compound preparation of ASU systems highlight the efficacy on various liver disorders. But well planned clinical trials to establish the safety and efficacy is the need. ASU medicines have an opportunity to develop new drugs and contribute as safe and cost effective treatment for Liver disorders.

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