Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

A Review on Hepatoprotective Activity of Medicinal Plants from Indian Origin and an Insight on Diagnosis and Treatment of Liver Diseases

Muslek Uddin Mazumder [1]* , George Hmangte Kom [1] , Pinku Bordoloi [1] , Narzin Nehar [1] , Siddhartha Sankar Das [1] , TC Lalhriatpuii [2] , Apurba Talukdar [1] , Bhargab Jyoti Sahariah [1]

[1] NETES Institute of Pharmaceutical Science, Kamrup, Assam, India 781125

[2] Regional Institute of Paramedical and Nursing Sciences, Aizawl, Mizoram, India 796017

***Corresponding Author:**

Muslek Uddin Mazumder

Assistant Professor, NETES Institute of Pharmaceutical Science, Kamrup, Assam, India

(Received: 14 April 2024 Revised: 1 May 2024 Accepted: 18 June 2024)

KEYWORDS

Hepatoprotective activity, biopsy, medicinal plant, HVPG, *Silybum marianum.*

ABSTRACT:

Liver is one of the vital organs responsible for metabolism in the body. Liver performs various functions including synthesis of clotting factors and other proteins, deactivation of harmful chemicals and elimination of bile salts. Liver injury leads to formation of different diseases like cirrhosis, fibrosis, hepatocellular carcinoma and fatty liver diseases. Chronic liver diseases are associated with various risk factors leading to different pathological conditions. Early diagnosis of the chronic liver disease is of utmost important for proper management of liver diseases for limiting the progression diseases to a greater extent. Diagnosis of the liver disease includes both invasive and non-invasive methods. Treatment and management of the liver diseases includes both medication therapy and preventive measures. In this study, different plants from Indian origin were studied for mitigation of liver diseases and different parts of these plants are utilized for the hepatoprotective activity. This review work will help the researchers to explore these plants for designing of new chemical compounds for the treatment of various liver related disorders.

Introduction

Liver is one of the most vital organs present in the body. It is vital for regulating different physiological functions. It is also engaged in a number of essential processes, including metabolism, secretion, and storage[1]. Bile, which the liver manufactures and secretes, plays a crucial function in digestion[2]. The liver is the biggest gland in the human body which is located in the upper right part of abdomen. Hepatocytes are liver cells that perform important functions in the body such as protein and bile synthesis, glycogen, vitamin, and iron storage, and toxic chemical and drug metabolism. Drug metabolism is a process detoxification in which a substance is chemically changed to a lesser toxic form by an enzymatic system.[3]

The important health issue of liver malfunction or injury presents difficulties for the pharmaceutical business, medication regulatory organizations, and healthcare practitioners[4]. Non-alcoholic fatty liver disease (NAFLD) causes most of the liver disease in the world. Acute or chronic hepatitis (inflammation), hepatosis (non-inflammatory liver disease), and cirrhosis (degenerative disorder resulting in liver fibrosis) are the three types of liver ailments that continue to be an issue for the world's health[5]. Numerous crucial innate and adaptive (acquired) immune system functions are carried out by the liver[6]. Viral hepatitis (hepatitis A, B, C, and D), autoimmune liver disease (AIH, PBC), alcoholism, non-alcoholic steatohepatitis (NASH), drug-induced liver injury, liver tumour, non-alcoholic fatty liver disease (NAFLD), liver transplantation, and liver cirrhosis are among the different liver illnesses. NAFLD

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

is a condition that primarily affects adults in their middle to late years [7]. Prevalence, incidence, progression, and consequences of NAFLD and NASH were calculated worldwide[8].

The only treatment now available for terminal liver failure is liver transplantation[9]. Regardless of the cause of the liver illness, liver cirrhosis is the most important risk factor for the generation of hepatocellular carcinoma (HCC)[10]. Different liver damage mechanisms that cause necroinflammation and fibrogenesis result in liver cirrhosis[11]. Aging increases the prevalence of several liver diseases, and older patients experience advanced liver disease more frequently than younger patients. NAFLD prevalence rates are estimated as 29% in the USA, 15–20% in central America, 26% in Mexico and 28% in Belize and Barbados depemding on the prevalence of obesity[12].

The management of human health is greatly influenced by medicinal plants. According to WHO (1993), traditional medicine, which is mostly based on plant material, is used by about 80% population of the world[5]. There are numerous medicinal plants found in various regions of India that have been identified as hepatoprotective medications and are frequently used to treat liver problems. Numerous plants and polyherbal preparations exhibit hepatoprotective properties; about 160 phytochemicals and other phytoconstituents have been asserted to possess this property[13]. Medicinal plants coontribute an important part in human health care. Approximately 80% of the world's population relies on plant based traditional medicine for the treatment. Traditional medicine encompasses a variety of ancient health care practises of natural origin such as folk/tribal practises, Ayurveda, Siddha, Amchi, and Unani[14].

Liver diseases can be life threatening, carrying a serious threat to global public health. As a result, there has been a lot of interest in complementary and alternative medicines for treating hepatic disorders. The utilization of herbs as medicines to treat liver diseases has increased worldwide, because of the widespread belief that they are safe and free of serious side effects. Furthermore, they are promptly available and easily obtained from nature[15]. To develop a remarkable herbal agent to treat various liver diseases, medicinal plants must be validated for properties such as liver regeneration, antihepatotoxic activity, and antiviral activity[16].

Table 1 Medicinal Plants containing hepatoprotective activities from Indian Origin

Sl. no	Biological name	Local name	Family	Part used	Active constituent	References
1	*Amaranthus caudatus Linn*	Tassel flower	Amaranthaceae	Whole plant	Flavonoids, saponins, glycosides	[17]
2	*Anisochilus carnosus Linn*	Thick leaved lavender	Lamiaceae	stems	Alkaloids, flavonoides, glycosides	[18]
3	*Asparagus racemosus Linn*	Satawar	Asparagaceae	Roots	Phenols, coumarins	[19]
4	*Azima tetracantha*	Bee sting bush	Salvadoracaceae	Leaves	Flavonoides ,triterpenoides	[20]

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

5	*Calotropis procera*	Rubber bush	Asclepediaceae	Root bark	Terpinoids glycosides, flavonoides	[21]
6	*Cajanus cajan Linn*	Pigeon pea	Leguminosae	Pigeon pea leaf	Flavonoides ,stibenes	[22]
7	*Cajanus scarabaeoides Linn*	Pigeonpea	Fabaceae	Whole plant	flavonoids	[23]
8	*Carissa carindas Linn*	Karandang	Apocyanaceae	Root	Alkaloids, tannins, steroids	[24]
9	*Clitoria ternatea Linn*	Butterfly pea	Fabaceae	Leaves	Phenolic flavonoides	[25]
10	*Ficus religiosa*	Sacred fig tree	Moraceac	Steam bark	Glycoside, steroids, tannins	[26]
11	*Coccinia indica*	Kovai	Cucurbitaceae	leaves	Glycoside, flavonoid, alkaloids, phenol	[27]
12	*Wedelia chinensis*	Bhangra and pilabhangra	Asteraceae	Whole plant	Flavonoids, diterpenes, saponins	[28]
13	*Flacourtia indica*	Ramontchi	Salicaceae	Aerial part	Ferulic acid, caffeic acid, vanillic acid	[29]
14	*Silybum marianum*	Milk thistle	Asteraceae	fruits	Silibinin, flavonolignan	[30]
15	*Matricaria chamomilla*	Chamomile	Asteraceae	flower	Chamazulene, bisabolol	[31]

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

16	*Coccinia grandis*	Ivy gourd	Curcubitaceae	fruits	Giycosides alkaloids, flavonoid, terpenoides, phenol	[32]
17	*Aegle marmelos*	Bael	Rutaceae	fruits	Imperatorin, psoralen	[33]
18	*Cassia roxburghii*	Red cassia	Fabaceae	seeds	Hexacosanol, 1-octacosanol, palmitic acid	[34]
19	*Orthosiphan stamineus*	Java tea	Lamiaceae	Leaves	Rosmarinic acid, sinensetin , eupatorin	[35]
20	*Ficus carica*	Common fig	Moraceae	Leaves	Benzyl aldehyde, benzyl alcohol, furanoid	[36]
21	*Lepidium sativum*	Garden cress	Brassicaceae	Leaves	Glycosides, flavonoids, cardiotonic glycosides	[37]
22	*Solanum nigram*	kakahva	Solanaceae	Fruits	Solamargine ,solasonine solanine	[38]
23	*Amaranthus tricolor linn.*	Edible amaranth	Amaranthaceae	Roots	Salicylic acid, gallic acid, syringic acid	[39]
24	*Luffa echinata*	Akhuvishaka	Cucurbitaceae	Fruits	Cucurbitacin, saponin, echinsatin	[40]

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

25	*Dichrostachys cinerea*	Sicklebush	Mimoseae	Leaves	Flavonoides , tannins, sterols, triterpenes	[41]
26	*Cassia fistula*	Golden shower	Fabaceae	Leaf	Rhein, triterpenes, sugar	[42]
27	*Azadirachta indica*	Neem	Meliaceae	Leaf	N[37]imbolinin , nimbin , nimbidin	[43]
28	*Polygala arvensis*	Field milkwort	Polygalaceae	Leaves	Triglycerides, l-lactate dehydrogrnase	[44]
29	*Acacia ctechu*	Black cutch	Fabaceae	Seed /bark	Catechin	[45]
30	*Achillea millefolium*	Yarrow	Asteraceae	leaves	Achilline	[46]
31	*Adhatoda vasica*	Malabar nut	Acanthaceae	Leaf	Vasicine	[47]
32	*Aloe indica*	Aloe vera	Lilaceae	Leaf	Aloin	[48]
33	*Centella asiatica*	Gotu kola	Apiaceae	leaves	Hydrocotyline	[49]
34	*Cichorium intybus*	Chicory	Asteraceae	Root/flower	Sesquiterpene lactones	[50]
35	*Curcuma longa*	Turmeric	Zingiberaceae	Root	Curcumin	[51]
36	*Fumaria indica*	Fumitory	papaveraceae	Whole plant	Monomethyl fumarate	[52]
37	*Embelia ribes*	Vidanga	Myrsinaceae	fruits	Embelin	[53]
38	*Glycyrrhiza glabra*	Liquoeice	Fabaceae	Root	Glycyrrhizin	[54]
39	*Piper longum*	Long pepper	Piperaceae	Root/stem	Piperine	[55]
40	*Ocimum sanctum*	Tulsi	Lamiaceae	leaves	Ursolic acid, eugenol	[56]

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

41	*Andrographis paniculata*	Nees	Acanthaceae	Whole plant	Diterpenoids, flavonoids and polyphenols	[57]
42	*Careya arborea*	Wild guava	Lecythidaceae	Bark	Flavonoids, tannins, alkaloids	[58]
43	*Eclipta alba*	False daisy	Asteraceae	Root	Coumestan	[59]
44	*Morinda citrifolia*	Noni	Rubiaceae	Leaf	Morindone	[60]
45	*Pterocarpus santalinus*	Red sanders	Fabaceae	Heartwood,Bark	Phenol,alcohol,ethers, ketone	[61]
46	*Phyllanthus reticulates*	Black – honey shrub	phyllanthaceae	Root	Tannic acid, terpenoids	[62]
47	*Cleome viscose Linn*	Hurhur	capparaceae	Leaf	Palmitic acid, stearic acid, oleic acid	[63]
48	*Phyllanthus amarus*	Carry	Phyllanthaceae	Leaf	Phyllanthin, corillagin	[64]
49	*Phyllanthus emblica*	Indian goose berry	Phyllanthaceae	Fruits	Triacontanol, triacontanoic acid	[65]
50	*Andrographis lineata*	Waterwillow	Acanthaceae	Leaf	Diterpenoids, flavonoids, polyphenols	[66]
51	*Tinospora cordifola*	Guduchi	Menspermaceae	Leaf	Giloin, gilenin	[67]
52	*Withania somnifera*	Aswagandha	Solanaceae	Leaf	Withaferin	[68]
53	*Sida cordifolia*	Bala	Malvaceae	Root	Fumaric acid	[69]

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

54	*Tamarix gallica*	Manna plant	tamaricaceae	Leaves	Tannin	[70]
55	*Terminalia chebula*	Chebulic myrobalan	Combretaceae	Fruit	Glycoside, tannin	[71]
56	*Silybum marianum*	Milk thistle	Asteraceae	Seed	Silymarin	[72]
57	*Picrorhiza kurroa*	Picrorhiza	Plantaginaceae	Root	Picroside I, d-mannitol	[73]
58	*Emblica officinalis*	Indian gooseberry	Phyllanthaceae	Fruit	Gallic acid, ascorbic acid, ellagic acid	[74]
59	*Swertia chirayita*	Chirata	Gentianaceae	Plant	Glycoside, phenols	[75]
60	*Tecomella undulata*	Desert teak	Bignoniaceae	Stem bark	Lapachol	[76]
61	*Taraxacum officinale*	Dandelion	Asteraceae	Leaves	Taraxasterol	[77]
62	*Crocus sativus*	Saffron	Iridaceae	Flower	Crocin, safranal	[78]
63	*Urtica parviflora*	Nettle	Urticaceae	Leaves	Fatty acids, alkaloids, terpenoids	[79]
64	*Woodfordia fruticosa*	Fire flame bush	Lythraceae	Flower	Tannins, flavonoides, glycosides	[80]
65	*Nardostacys jatamansi*	Jatamansi	Valerianceae	Rhizomes	Jatamansone, jatamanshic acid	[81]
66	*Hedychium spicatum*	Kapur kachri	Zingiberaceae	Rhizomes	Alpha- pinene, limonene	[82]
67	*Cinnamomum verum*	Cinnamon	Lauraceae	Bark	Cinnamaldehyde, eugenol	[83]
68	*Berberis aristata*	Daruhaldhi	Berberidaceae	Leaves	Berberine	[84]

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

69	*Nerium oleander Linn*	Oleander	Apocynaceae	Flower	Alkaloids, flavonoids, tannins, glycosides	[85]
70	*Camellia sinensis*	Tea	Theaceae	Leaves	Epigallocatechin galate	[86]

DIAGNOSIS OF LIVER DISEASES

Due to high risk of likelihood of advanced liver diseases and condition like hepatocellular carcinoma, there is urgent need of early detection of liver disease at a stage of effective therapeutic intervention. Involvement of surveillance by regular screening of individuals possessing higher risk of development of liver diseases[87]. Various diagnostic techniques were developed to access an early and reliable detection for liver diseases. These techniques includes both invasive and non-invasive procedures[88]. Figure 1 demonstrated different diagnostic methods for liver diseases.

Liver biopsy: Biopsy is an useful in the diagnostic tool for individuals with abnormal liver tests with unknown causes or patients with a specific liver condition has been suspected but confirmation is not done. Examples include patients suffering from genetic ailments such as Niemann-Pick disease, Wilson disease, α-1-antitrypsin disease, glycogen storage diseases, tyrosinemia, amyloidosis, glycogen storage diseases, etc[89].

Laparoscopy: Gastroenterologists frequently use the antiquated laparoscopy procedure. It is safe and comfortable to perform on patients under sedation and local anesthesia[90]. Laparoscopy is a minimally invasive treatment that allows for the visualization of the inside components of any organ. During the procedure, a gas-filled peritoneal cavity is initially created, and the contents are then inspected using a hard telescope (laparoscope) that is introduced via a hole in the organ's wall. After positioning the telescope, it is possible to perform different surgical or diagnostic procedures by inserting different surgical instruments, like biopsy forceps, into adjacent apertures[91].

HVPG measurement*:* The hepatic venous pressure gradient (HVPG) is the best way to measure portal hypertension in liver sickness, and testing for HVPG in cirrhotic patients provides independent predictive data on survival and decompensation risk. Measuring HVPG is also useful in evaluating persons with compensated chronic liver disease or hepatocarcinoma for the risk of liver failure and death following liver resection. The most likely to benefit from treatment patients with portal hypertension can be identified based on their HVPG response to pharmaceutical therapy[92].

Endoscopy: Endoscopy should be made available to those who meet the appropriate criteria since it can be utilized for variceal screening and therapy, as well as for the diagnosis of previously undiagnosed liver illnesses. People suffering from liver illness can be difficult to sedate, and as more patients have liver transplants and new endoscopic model like capsule endoscopy and endoscopic ultrasound (EUS) are developed, the difficulty of endoscopy in liver disease continues to increase[93].

Imaging techniques: Hepatic ultrasonography and magnetic resonance imaging (MRI) are popularly being used for the authentication, characterization, and evaluation of the response to treatment of focal and diffuse liver diseases. Even now, ultrasonography is the first choice of examination[94]. Imaging methods have developed to a high degree of precision and sophistication when a patient is being assessed for a possible liver issue[95].

Serum Markers: Hepatic fibrosis serum markers might be either direct or indirect indicators. Indirect markers, such as transaminases, coagulation factors, and platelet count, indicates the condition liver normal function. Direct indicators of fibrosis represent the turnover of extracellular matrix. Procollagen I C terminal, procollagen III N terminal, tenascin, tumour growth factor, and tissue inhibitor of metalloproteinases are all markers of matrix deposition. Procollagen IV C peptide, procollagen IV N peptide, collagen IV,

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

hydroxylysypyridinoline, urine desmosine, and Undulin, matrix metalloproteinases are all indications of matrix clearance[96].

Artificial Intelligence (AI): Machine Learning Algorithm (MLA) can be utilized for estimation HVPG with significant accuracy. Artificial neural networks (ANN) designed on platelet count, portal vein diameter and spleen width determine the presence of esophageal varices with marked accuracy, specificity and sensitivity[97]. The use of AI based prediction model for the analysis prognosis of liver diseases can be helpful to a larger extent and provide an additional source for the diagnosis of disease for the healthcare professionals[98].

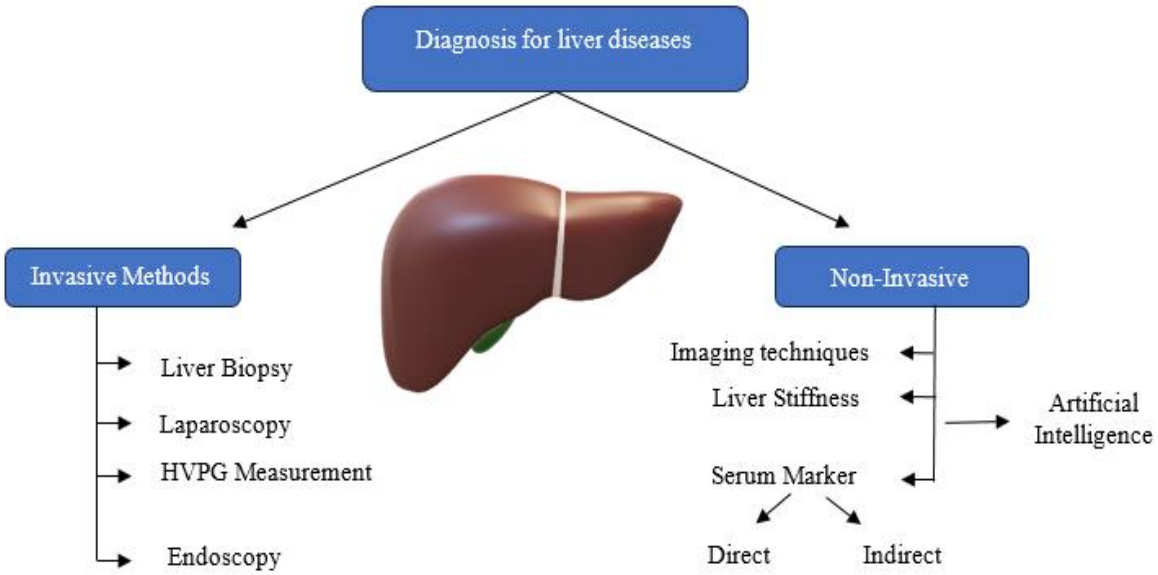

Figure 1. Different diagnostic methods for liver diseases

TREATMENT:HEPATOPROTECTIVE ACTIVITY

There are limited treatment alternatives for common liver conditions like cirrhosis, fatty liver, and chronic hepatitis. Treatments like interferon, colchicine, corticosteroids, and penicillamine have a different rate of success and a higher possibilities of side effects[99]. To prevent liver fibrosis and subsequent deterioration of hepatic features, specific treatment is needed. It entails eliminating the underlying causes of the illness[100]. Figure 2 illustrates the different treatment protocol for management of liver diseases.

Lifestyle modification

Nutritional changes focused at caloric restriction and weight loss, macronutrient shift, and body interest are subcategories of lifestyle modification. The two main types of physical interest are aerobic and resistive[101]. It comprised of food, exercise, and weight loss has been promoted to treat individuals with NAFLD[102].

Exercise and physical activity

Resistance training causes muscle damage, regeneration, and protein synthesis resulting in an increase in skeletal muscle tissues[103]. Exercise increases motivational capacity but may not necessarily stop sarcopenia. Resistance and patience exercises have the ability to increase muscular mass and functional capacity[104].

Ammonia lowering strategies

Non-absorbable disaccharides and antibiotics that stop ammonia from building up in the gut are two current methods for lowering ammonia[105]. Reversal of the hepatic encephalopathy and a reduction in blood ammonia levels are the main outcomes of such therapy. However, it is widely acknowledged that blood ammonia

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

levels do not necessarily correlate with the extent of hepatic encephalopathy, the most researched response[106]. Use of mobile permeable esters of 2-ketoglutarate (KG), which can offer an immediate anaplerotic inflow with elimination of ammonia as glutamine, is one of the new and effective ways to lower muscle ammonia. However, breakdown of glutamine will subsequently become constrained, and protection of skeletal muscle will depend on long-term disposal of ammonia. Because they can prevent formation of one mole of ammonia for each mole of amino acid, isoleucine and valine were recommended as anaplerotic substrates. However, the molecular and practical reaction to these interference have not yet been assessed in preclinical or scientific investigations to reduce ammonia or counteract sarcopenia[104].

Omega-3-polyunsaturated fatty acid (PUFA) supplementation

Supplementation with Omega-3-polyunsaturated fatty acid (PUFA) improves the live fat, Insulin resistance, triglycerides, alanine transaminase (ALT), aspartate transaminase (AST), γ-glutamyl transferase, and Glucose in patients suffering from NAFLD. Reduction in liver fat and these enzymes suggest that supplementation with ω-3-polyunsaturated fatty acid can improve the liver health. ω-3-polyunsaturated fatty acid also improves the total cholesterol, High density lipoprotein including Body Mass Index[107], [108].

Coffee intake

Twenty years ago, it was shown that drinking coffee decreased the risk of developing liver disease in cirrhotic alcoholic patients. Amount of the liver enzymes like alanine transaminase (ALT), aspartate transaminase (AST), and γ-glutamyltransferase have been found to be inversely correlated with increasing coffee consumption[109].

Liver transplantation

After the host liver has been removed, the liver can be transplanted as an additional (auxiliary) organ either at the orthotopic site or at the ectopic site. The diseased organ is removed during an orthotopic liver transplant and replaced with a cadaveric liver as anatomically normal as feasible[110]. For the replacement of a markedly damaged liver in patients with less recovery chances from acute paediatric liver failure (PALF), liver transplantation (LT) is the best alternative option of therapy. But this is complicated by the effects of protracted immunosuppressive reaction. Another method of transplantation, Auxiliary partial liver orthotopic transplantation (APOLT), which provides a graft that ensures the normal function of liver until the regeneration of the native liver takes, it has emerged as a potential better technique possible progression to immunosuppression withdrawal[111].

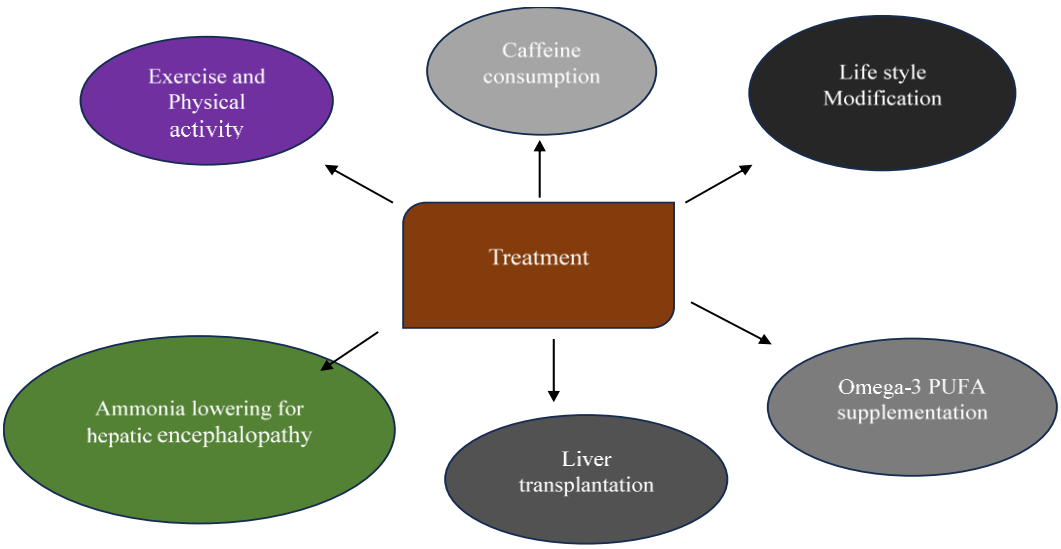

Figure 2. Treatment for liver diseases

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

CONCLUSION

Acute and Chronic liver diseases are prevailing in the world concerning the global health issues and reducing the quality of life in mass population. Various liver diseases like hepatocellular carcinoma, cirrhosis, viral hepatitis, non-alcoholic steatohepatitis, non-alcoholic fatty liver disease are required to be treated promptly as liver is an important organ of metabolic importance. Therefore, early detection of these diseases is prime action in treatment and management of the diseases for reduction in the severity. The diagnosis of liver disease includes both invasive and non-invasive methods. Non-invasive methods are more convenient and widely used by the physicians. Treatment of liver diseases employs various drugs and also some preventive therapies. Artificial Intelligence based diagnosis is also useful for detection as well as management of liver disease prognosis. However, standardization of the method of diagnosis is necessary for the use of artificial intelligence. Plants were also explored for their hepatoprotective activities. Different parts of the plants are utilized in various studies suggest that plant-based formulation can be used for treatment of liver diseases. Phytochemicals present in plant are mainly responsible for hepatoprotective activity. This review work will help to provide insights of knowledge regarding utilization of different plants parts (**Table 1.**) for mitigation of liver diseases and also provide an overview on diagnostic methods and management of the liver related ailments. Early diagnosis of liver diseases and management of diseases with the help of medication therapy or plant derived compounds will reduce the burden of the disease in the global prospect.

STATEMENT OF ETHICS

No human or animals were used in this study by any author.

CONFLICT OF INTERESTS STATEMENT

Authors declare no conflict of interests related to this study.

REFERENCES

[1] E. A. Adewusi and A. J. Afolayan, “A review of natural products with hepatoprotective activity,” *Journal of Medicinal Plants Research*, vol. 4, pp. 1318–1334, 2010.

[2] S. Bhawna and S. U. Kumar, “Hepatoprotective activity of some indigenous plants,” *Int J Pharmtech Res*, vol. 1, no. 4, pp. 1330–1334, 2009.

[3] V. Bhaargavi, G. S. L. Jyotsna, and R. Tripurana, “a Review on Hepatoprotective Activity,” *Int J Pharm Sci Res*, vol. 5, no. 3, pp. 690–702, 2014, doi: 10.13040/IJPSR.0975-8232.5(3).690-02.

[4] Mohamed Saleem T S, Madhusudhana Chetty C, Ramkanth S, Rajan V S T, Mahesh Kumar K, and Gauthaman K, “Hepatoprotective Herbs – A Review,” *International Journal of Research in Pharmaceutical Sciences*, vol. 1, no. 1 SE-Review Article, pp. 1–5, Jan. 2010.

[5] M. Asadi-Samani, N. Kafash-Farkhad, N. Azimi, A. Fasihi, E. Alinia-Ahandani, and M. Rafieian-Kopaei, “Medicinal plants with hepatoprotective activity in Iranian folk medicine,” *Asian Pac J Trop Biomed*, vol. 5, no. 2, pp. 146–157, 2015, doi: 10.1016/S2221-1691(15)30159-3.

[6] V. Vilas-Boas *et al.*, “Primary hepatocytes and their cultures for the testing of drug-induced liver injury.,” *Adv Pharmacol*, vol. 85, pp. 1–30, 2019, doi: 10.1016/bs.apha.2018.08.001.

[7] K. Tajir and Y. Shimizu, “Liver physiology and liver diseases in the elderly,” *World J Gastroenterol*, vol. 19, no. 46, pp. 8459–8467, 2013, doi: 10.3748/wjg.v19.i46.8459.

[8] Z. M. Younossi, A. B. Koenig, D. Abdelatif, Y. Fazel, L. Henry, and M. Wymer, “Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes.,” *Hepatology*, vol. 64, no. 1, pp. 73–84, Jul. 2016, doi: 10.1002/hep.28431.

[9] T. Liu, Y. Zhou, K. S. Ko, and H. Yang, “Interactions between Myc and Mediators of Inflammation in Chronic Liver Diseases.,” *Mediators Inflamm*, vol. 2015, p. 276850, 2015, doi: 10.1155/2015/276850.

[10] K. Tarao *et al.*, “Real impact of liver cirrhosis on the development of hepatocellular carcinoma in various liver diseases-meta-analytic assessment.,” *Cancer Med*, vol. 8, no. 3, pp. 1054–1065, Mar. 2019, doi: 10.1002/cam4.1998.

[11] E. A. Tsochatzis, J. Bosch, and A. K. Burroughs, “Liver cirrhosis.,” *Lancet*, vol. 383, no. 9930, pp.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

1749–1761, May 2014, doi: 10.1016/S0140-6736(14)60121-5.

[12] J. A. López-Velázquez *et al.*, "The prevalence of nonalcoholic fatty liver disease in the Americas.," *Ann Hepatol*, vol. 13, no. 2, pp. 166–178, 2014.

[13] R. Srivastava and P. Srivastava, "Hepatotoxicity and the Role of Some Herbal Hepatoprotective Plants in Present Scenario," *International Journal of Digestive Diseases*, vol. 04, Jan. 2018, doi: 10.4172/2472-1891.100034.

[14] H. Kumar, A. Ramesh, J. N. Suresh Kumar, B. Mohammed Ishaq, and C. H. Kumar, "a Review on Hepatoprotective Activity of Medicinal Plants," vol. 2, no. 3, pp. 501–515, 2011.

[15] S. A. Ali, N. H. Sharief, and Y. S. Mohamed, "Hepatoprotective Activity of Some Medicinal Plants in Sudan," *Evidence-based Complementary and Alternative Medicine*, vol. 2019, 2019, doi: 10.1155/2019/2196315.

[16] D. Jain, P. Chaudhary, A. Kotnala, R. Hossain, K. Bisht, and M. N. Hossain, "Hepatoprotective activity of medicinal plants: A mini review," *Journal of Medicinal Plants Studies*, vol. 8, no. 5, pp. 183–188, 2020, doi: 10.22271/plants.2020.v8.i5c.1212.

[17] B. S. Ashok Kumar *et al.*, "Hepatoprotective activity of methanol extract of Amaranthus caudatus Linn. against paracetamol-induced hepatic injury in rats.," *Zhong Xi Yi Jie He Xue Bao*, vol. 9, no. 2, pp. 194–200, Feb. 2011, doi: 10.3736/jcim20110213.

[18] J. Cao, Y. Zheng, X. Xia, Q. Wang, and J. Xiao, "Total flavonoid contents, antioxidant potential and acetylcholinesterase inhibition activity of the extracts from 15 ferns in China," *Ind Crops Prod*, vol. 75, pp. 135–140, 2015, doi: 10.1016/j.indcrop.2015.04.064.

[19] A. Al Mamun *et al.*, "Comparison of the hypoglycemic, hypolipidemic and hepatoprotective effects of Asparagus racemosus Linn. in combination with gliclazide and pioglitazone on alloxan-induced diabetic rats," *Pharmacol Pharm*, vol. 8, no. 02, pp. 52–74, 2017.

[20] T. N. Begum, M. H. M. Ilyas, and A. V. Anand, "Hepatoprotective activity of Azima tetracantha Lam. in experimental animals," *J Pharm Res*, vol. 4, no. 7, pp. 2359–2360, 2011.

[21] A. Basu, T. Sen, R. N. Ray, and A. K. N. Chaudhuri, "Hepatoprotective effects of Calotropis procera root extract on experimental liver damage in animals.," *Fitoterapia*, vol. 63, no. 6, pp. 507–514, 1992.

[22] J. C. Gogoi, D. Mohanta, and P. K. Borah, "Hepatoprotective activity of averrhoa carambola, Cajanus cajan and paederia foetida against acetaminophen and D-galactosamine induced hepatotoxicity in rats," *Journal of Pharmaceutical Research*, pp. 76–80, 2010.

[23] S. Pattanayak, S. S. Nayak, D. P. Panda, S. C. Dinda, V. Shende, and A. Jadav, "Hepatoprotective activity of crude flavonoids extract of Cajanus scarabaeoides (L) in paracetamol intoxicated albino rats," *Asian J Pharm Biol Res*, vol. 1, no. 1, pp. 22–27, 2011.

[24] P. Bhati, A. Shukla, and M. Sharma, "Hepatoprotective activity of leaves extracts of Carissa carandas Linn," *American Journal of Pharm Research*, vol. 4, no. 11, pp. 5185–5192, 2014.

[25] K. Nithianantham *et al.*, "Evaluation of hepatoprotective effect of methanolic extract of Clitoria ternatea (Linn.) flower against acetaminophen-induced liver damage," *Asian Pac J Trop Dis*, vol. 3, no. 4, pp. 314–319, 2013.

[26] S. A. Parameswari, C. M. Chetty, and K. B. Chandrasekhar, "Hepatoprotective activity of Ficus religiosa leaves against isoniazid+ rifampicin and paracetamol induced hepatotoxicity," *Pharmacognosy Res*, vol. 5, no. 4, p. 271, 2013.

[27] B. S. Kumar, D. Gnanasekaran, V. Jaishree, and K. P. Channabasavaraj, "Hepatoprotective activity of Coccinia indica leaves extract," *Int J Pharm Biomed Res*, vol. 14, pp. 154–156, 2010.

[28] A. K. Sharma *et al.*, "Hepatoprotective effects of Wedelia calendulacea," *J Ethnopharmacol*, vol. 25, no. 1, pp. 93–102, 1989.

[29] M. Nazneen, M. A. Mazid, J. K. Kundu, S. C. Bachar, F. Begum, and B. K. Datta, "Protective effects of Flacourtia indica aerial parts extracts against paracetamol-induced hepatotoxiciy in rats," *Journal of taibah university for science*, vol. 2, pp. 1–6, 2009.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

[30] M. Bahmani, H. Shirzad, S. Rafieian, and M. Rafieian-Kopaei, "Silybum marianum: beyond hepatoprotection," *J Evid Based Complementary Altern Med*, vol. 20, no. 4, pp. 292–301, 2015.

[31] S. Shebbo, M. El Joumaa, R. Kawach, and J. Borjac, "Hepatoprotective effect of Matricaria chamomilla aqueous extract against 1, 2-Dimethylhydrazine-induced carcinogenic hepatic damage in mice," *Heliyon*, vol. 6, no. 6, 2020.

[32] R. Vadivu, A. Krithika, C. Biplab, P. Dedeepya, N. Shoeb, and K. S. Lakshmi, "Evaluation of hepatoprotective activity of the fruits of Coccinia grandis Linn," *International Journal of Health Research*, vol. 1, no. 3, 2008.

[33] V. Singanan, M. Singanan, and H. Begum, "The hepatoprotective effect of bael leaves (Aegle marmelos) in alcohol induced liver injury in albino rats," *International Journal of Science & Technology*, vol. 2, no. 2, pp. 83–92, 2007.

[34] M. Asif, "Liver toxicity and role of herbal drugs as hepatoprotective agents: An overview," *Journal of Ethno-Pharmaceutical Products*, vol. 2, no. 2, pp. 1–20, 2021.

[35] C. Maheswari, R. Maryammal, and R. Venkatanarayanan, "Hepatoprotective activity of Orthosiphon stamineus on liver damage caused by paracetamol in rats," *Jordan J Biol Sci*, vol. 1, no. 3, pp. 105–108, 2008.

[36] N. Y. Gond and S. S. Khadabadi, "Hepatoprotective activity of Ficus carica leaf extract on rifampicin-induced hepatic damage in rats," *Indian J Pharm Sci*, vol. 70, no. 3, p. 364, 2008.

[37] A. Shukla and P. Bigoniya, "Hepatoprotective effect of Lepidium sativum Linn (Cruciferae) total alkaloid fraction against CCl4 induced hepatotoxicity on rats," *Research Journal of Pharmacognosy and Phytochemistry*, vol. 5, no. 2, pp. 94–99, 2013.

[38] K. Raju, G. Anbuganapathi, V. Gokulakrishnan, B. Rajkapoor, B. Jayakar, and S. Manian, "Effect of dried fruits of solanum nigrum L INN against CCl4-induced hepatic damage in rats," *Biol Pharm Bull*, vol. 26, no. 11, pp. 1618–1619, 2003.

[39] S. Aneja, M. Vats, S. Aggarwal, and S. Sardana, "Phytochemistry and hepatoprotective activity of aqueous extract of Amaranthus tricolor Linn. roots," *J Ayurveda Integr Med*, vol. 4, no. 4, p. 211, 2013.

[40] B. Ahmed, T. Alam, and S. A. Khan, "Hepatoprotective activity of Luffa echinata fruits," *J Ethnopharmacol*, vol. 76, no. 2, pp. 187–189, 2001.

[41] P. S. Babu, V. Krishna, K. R. Maruthi, K. Shankarmurthy, and R. K. Babu, "Evaluation of acute toxicity and hepatoprotective activity of the methanolic extract of Dichrostachys cinerea (Wight and Arn.) leaves," *Pharmacognosy Res*, vol. 3, no. 1, p. 40, 2011.

[42] T. Bhakta, S. Banerjee, S. C. Mandal, T. K. Maity, B. P. Saha, and M. Pal, "Hepatoprotective activity of Cassia fistula leaf extract," *Phytomedicine*, vol. 8, no. 3, pp. 220–224, 2001.

[43] R. Chattopadhyay, "Possible mechanism of hepatoprotective activity of Azadirachta indica leaf extract: part II," *J Ethnopharmacol*, vol. 89, no. 2–3, pp. 217–219, 2003.

[44] S. P. Dhanabal, G. Syamala, M. N. S. Kumar, and B. Suresh, "Hepatoprotective activity of the Indian medicinal plant Polygala arvensis on D-galactosamine-induced hepatic injury in rats," *Fitoterapia*, vol. 77, no. 6, pp. 472–474, 2006.

[45] P. Jayasekhar, P. V Mohanan, and K. Rathinam, "Hepatoprotective activity of ethyl acetate extract of Acacia catechu," *Indian J Pharmacol*, vol. 29, no. 6, p. 426, 1997.

[46] R. M. Al-Ezzy, R. S. A. Al Anee, and O. A. Kathum, "Hepatoprotective effects of Achillea millefolium methanolic extract on carbon tetrachloride induced hepatotoxicity on albino male mice," *International Journal of Advanced Research in Biological Sciences*, vol. 4, no. 8, pp. 98–109, 2017.

[47] D. Bhattacharyya, S. Pandit, U. Jana, S. Sen, and T. K. Sur, "Hepatoprotective activity of Adhatoda vasica aqueous leaf extract on D-galactosamine-induced liver damage in rats," *Fitoterapia*, vol. 76, no. 2, pp. 223–225, 2005.

[48] V. K. Gupta, N. J. Siddiqi, A. K. Ojha, and B. Sharma, "Hepatoprotective effect of Aloe vera against cartap-and malathion-induced toxicity in Wistar rats," *J Cell Physiol*, vol. 234, no. 10, pp. 18329–18343, 2019.

[49] V. Sivakumar, A. M. Sadiq, and S. D. Bharathi, "Hepatoprotective activity of Centella asiatica linn. against paracetamol induced liver damage in experimental animals," *Emergent Life Sciences Research*, vol. 4, pp. 19–26, 2018.

[50] S. Sultana, S. Perwaiz, M. Iqbal, and M. Athar, "Crude extracts of hepatoprotective plants, Solanum nigrum and Cichorium intybus inhibit free radical-mediated DNA damage," *J Ethnopharmacol*, vol. 45, no. 3, pp. 189–192, 1995.

[51] S. L. Baxla, R. H. Gora, P. Kerketta, N. Kumar, B. K. Roy, and P. H. Patra, "Hepatoprotective effect of Curcuma longa against lead induced toxicity in Wistar rats.," 2013.

[52] K. S. Rao and S. H. Mishra, "Hepatoprotective activity of the whole plants of Fumaria indica.," 1997.

[53] M. Bist and S. B. Prasad, "Embelia ribes: A valuable medicinal plant," *J Chem Pharm Res*, vol. 8, no. 4, pp. 1229–1233, 2016.

[54] R. Al-Razzuqi, F. H. Al-Jawad, J. A. Al-Hussaini, and A. Al-Jeboori, "Hepatoprotective effect of Glycyrrhiza glabra in carbon tetrachloride-induced model of acute liver injury," *J Phys Pharm Adv*, vol. 2, no. 7, pp. 259–263, 2012.

[55] S. S. Jalalpure, M. B. Patil, N. S. Prakash, K. Hemalata, and F. V Manvi, "Hepatoprotective activity of the fruits of Piper longum Linn," *Indian J Pharm Sci*, vol. 65, no. 4, pp. 363–366, 2003.

[56] R. R. Chattopadhyay, S. K. Sarkar, S. Ganguly, C. Medda, and T. K. Basu, "Hepatoprotective activity of Ocimum Sanctum leaf extract against Paracetamol included Hepatic damage in rats," *Indian J Pharmacol*, vol. 24, pp. 163–165, 1992.

[57] S. Subramaniam, H. B. Hedayathullah Khan, N. Elumalai, and S. Y. Sudha Lakshmi, "Hepatoprotective effect of ethanolic extract of whole plant of Andrographis paniculata against CCl4-induced hepatotoxicity in rats," *Comp Clin Path*, vol. 24, no. 5, pp. 1245–1251, 2015, doi: 10.1007/s00580-015-2067-2.

[58] N. Senthilkumar, S. Badami, S. H. Dongre, and S. Bhojraj, "Antioxidant and hepatoprotective activity of the methanol extract of Careya arborea bark in Ehrlich ascites carcinoma-bearing mice," *J Nat Med*, vol. 62, no. 3, pp. 336–339, 2008, doi: 10.1007/s11418-008-0237-0.

[59] A. K. Saxena, B. Singh, and K. K. Anand, "Hepatoprotective effects of Eclipta alba on subcellular levels in rats," *J Ethnopharmacol*, vol. 40, no. 3, pp. 155–161, 1993.

[60] R. A. Repi, J. Ngangi, and H. M. Sumampouw, "Hepatoprotective Activity Combination Between Morinda Citrifolia Linn (Mengkudu) Extract And Virgin Coconut Oil (VCO)," *J Biol Agric Healthc*, vol. 3, no. 13, pp. 160–166, 2013.

[61] B. K. Manjunatha, "Hepatoprotective activity of Pterocarpus santalinus Lf, an endangered medicinal plant," *Indian J Pharmacol*, vol. 38, no. 1, p. 25, 2006.

[62] R. Srirama *et al.*, "Hepatoprotective activity of Indian phyllanthus," *Pharm Biol*, vol. 50, no. 8, pp. 948–953, 2012.

[63] H. Singh, A. Mishra, and A. K. Mishra, "Cleome viscosa linn (Capparaceae): a review," *Pharmacognosy Journal*, vol. 7, no. 6, 2015.

[64] F. Naaz, S. Javed, and M. Z. Abdin, "Hepatoprotective effect of ethanolic extract of Phyllanthus amarus Schum. et Thonn. on aflatoxin B1-induced liver damage in mice," *J Ethnopharmacol*, vol. 113, no. 3, pp. 503–509, 2007.

[65] C. Z. Huang, Y. T. Tung, S. M. Hsia, C. H. Wu, and G. C. Yen, "The hepatoprotective effect of Phyllanthus emblica L. fruit on high fat diet-induced non-alcoholic fatty liver disease (NAFLD) in SD rats," *Food Funct*, vol. 8, no. 2, pp. 842–850, 2017, doi: 10.1039/c6fo01585a.

[66] B. Sangameswaran, T. C. Reddy, and B. Jayakar, "Hepatoprotective effect of leaf extracts of Andrographis lineata nees on liver damage caused by carbon tetrachloride in rats," *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*, vol. 22, no. 1, pp. 124–126, 2008.

[67] U. Spandana, S. L. Ali, T. Nirmala, M. Santhi, and S. S. Babu, "A review on Tinospora cordifolia," *International Journal of Current Pharmaceutical Review and Research*, vol. 4, no. 2, pp. 61–68, 2013.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

[68] E. P. Sabina *et al.*, "Hepatoprotective and antioxidant potential of Withania somnifera against paracetamol-induced liver damage in rats," *Int J Pharm Pharm Sci*, vol. 5, no. 2, pp. 648–651, 2013.

[69] A. Jain, S. Choubey, P. K. Singour, H. Rajak, and R. S. Pawar, "Sida cordifolia (Linn)," *J Appl Pharm Sci*, no. Issue, pp. 23–31, 2011.

[70] M. K. Urfi, M. Mujahid, Badruddeen, M. A. Rahman, and M. A. Rahman, "The role of Tamarix gallica leaves extract in liver injury induced by rifampicin plus isoniazid in Sprague Dawley rats," *J Diet Suppl*, vol. 15, no. 1, pp. 24–33, 2018.

[71] R. Jain, K. Nandakumar, V. Srivastava, S. K. Vaidya, S. Patet, and P. Kumar, "Hepatoprotective activity of ethanolic and aqueous extract of Terminalia belerica in rats," *Pharmacologyonline*, vol. 2, pp. 411–427, 2008.

[72] P. Govind and Y. P. Sahni, "A review on hepatoprotective activity of silymarin," *Int J res Ayurveda pharm*, vol. 2, no. 1, pp. 75–79, 2011.

[73] A. B. Vaidya *et al.*, "Picrorhiza kurroa (Kutaki) Royle ex Benth as a hepatoprotective agent--experimental & clinical studies.," *J Postgrad Med*, vol. 42, no. 4, p. 105, 1996.

[74] K. R. Thilakchand, R. T. Mathai, P. Simon, R. T. Ravi, M. P. Baliga-Rao, and M. S. Baliga, "Hepatoprotective properties of the Indian gooseberry (Emblica officinalis Gaertn): a review," *Food Funct*, vol. 4, no. 10, pp. 1431–1441, 2013.

[75] R. Nagalekshmi, A. Menon, D. K. Chandrasekharan, and C. K. K. Nair, "Hepatoprotective activity of Andrographis paniculata and Swertia chirayita," *Food and Chemical Toxicology*, vol. 49, no. 12, pp. 3367–3373, 2011.

[76] A. Khatri, A. Garg, and S. S. Agrawal, "Evaluation of hepatoprotective activity of aerial parts of Tephrosia purpurea L. and stem bark of Tecomella undulata," *J Ethnopharmacol*, vol. 122, no. 1, pp. 1–5, 2009.

[77] A. Singh, S. Malhotra, and R. Subban, "Dandelion (Taraxacum officinale)-hepatoprotective herb with therapeutic potential," *Pharmacogn Rev*, vol. 2, no. 3, p. 163, 2008.

[78] H. Riaz *et al.*, "Hepatoprotective effect of Crocus sativus on amiodarone-induced liver toxicity," *Br J Pharm Res*, vol. 12, no. 4, 2016.

[79] M. Sarma Kataki, V. Murugamani, A. Rajkumari, P. Singh Mehra, D. Awasthi, and R. Shankar Yadav, "Antioxidant, hepatoprotective, and anthelmintic activities of methanol extract of Urtica dioica L. leaves," *Pharm Crop*, vol. 3, no. 1, 2012.

[80] B. K. Chandan *et al.*, "Hepatoprotective activity of Woodfordia fruticosa Kurz flowers against carbon tetrachloride induced hepatotoxicity," *J Ethnopharmacol*, vol. 119, no. 2, pp. 218–224, 2008.

[81] S. Ali, K. A. Ansari, M. A. Jafry, H. Kabeer, and G. Diwakar, "Nardostachys jatamansi protects against liver damage induced by thioacetamide in rats," *J Ethnopharmacol*, vol. 71, no. 3, pp. 359–363, 2000.

[82] G. K. Choudhary and S. P. Singh, "In vitro hepatoprotective efficacy of extract of Hedychium spicatum rhizome in paracetamol induced toxicity in HepG2 cell line," *Indian J. Anim. Sci*, vol. 88, pp. 546–549, 2018.

[83] K. Arun *et al.*, "Hepatoprotective Activity Of Cinnamon Zeylanicum Leaves Against Alcohol Induced Albino Rats," *Journal of Enggineering Research and Applications*, vol. 4, no. 8, pp. 177–184, 2014.

[84] K. Paudel, A. Ramamurthy, and G. Sharma, "REVIEW ON HEPATOPROTECTIVE EFFECT OF BERBERIS ARISTATA DC.," *Authorea Preprints*, 2022.

[85] K. G. Singhal and G. Das Gupta, "Hepatoprotective and antioxidant activity of methanolic extract of flowers of Nerium oleander against CCl4–induced liver injury in rats," *Asian Pac J Trop Med*, vol. 5, no. 9, pp. 677–685, 2012.

[86] P. Lodhi, N. Tandan, N. Singh, D. Kumar, and M. Kumar, "Camellia sinensis (L.) Kuntze extract ameliorates chronic ethanol-induced hepatotoxicity in albino rats," *Evidence-based complementary and alternative medicine*, vol. 2014, 2014.

[87] H. Wazir *et al.*, "Diagnosis and Treatment of Liver Disease: Current Trends and Future Directions.," *Cureus*, vol. 15, no. 12, p. e49920, Dec. 2023, doi: 10.7759/cureus.49920.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

[88] S. Mueller and L. Sandrin, "Liver stiffness: a novel parameter for the diagnosis of liver disease," *Hepat Med*, vol. 2, no. null, pp. 49–67, May 2010, doi: 10.2147/hmer.s7394.

[89] D. C. Rockey, S. H. Caldwell, Z. D. Goodman, R. C. Nelson, and A. D. Smith, "Liver biopsy.," *Hepatology*, vol. 49, no. 3, pp. 1017–1044, Mar. 2009, doi: 10.1002/hep.22742.

[90] L. R. F. Crantock, J. F. Dillon, and P. C. Hayes, "Diagnostic laparoscopy and liver disease: experience of 200 cases," *Aust N Z J Med*, vol. 24, no. 3, pp. 258–262, Jun. 1994, doi: https://doi.org/10.1111/j.1445-5994.1994.tb02169.x.

[91] E. Monnet and D. C. Twedt, "Laparoscopy.," *Vet Clin North Am Small Anim Pract*, vol. 33, no. 5, pp. 1147–1163, Sep. 2003, doi: 10.1016/s0195-5616(03)00058-5.

[92] J. Bosch, J. G. Abraldes, A. Berzigotti, and J. C. García-Pagan, "The clinical use of HVPG measurements in chronic liver disease.," *Nat Rev Gastroenterol Hepatol*, vol. 6, no. 10, pp. 573–582, Oct. 2009, doi: 10.1038/nrgastro.2009.149.

[93] C. Krystallis, G. S. Masterton, P. C. Hayes, and J. N. Plevris, "Update of endoscopy in liver disease: more than just treating varices.," *World J Gastroenterol*, vol. 18, no. 5, pp. 401–411, Feb. 2012, doi: 10.3748/wjg.v18.i5.401.

[94] B. E. Van Beers, J.-L. Daire, and P. Garteiser, "New imaging techniques for liver diseases.," *J Hepatol*, vol. 62, no. 3, pp. 690–700, Mar. 2015, doi: 10.1016/j.jhep.2014.10.014.

[95] M. Pinzani, K. Rombouts, and S. Colagrande, "Fibrosis in chronic liver diseases: diagnosis and management.," *J Hepatol*, vol. 42 Suppl, no. 1, pp. S22-36, 2005, doi: 10.1016/j.jhep.2004.12.008.

[96] L. Chrostek and A. Panasiuk, "Liver fibrosis markers in alcoholic liver disease.," *World J Gastroenterol*, vol. 20, no. 25, pp. 8018–8023, Jul. 2014, doi: 10.3748/wjg.v20.i25.8018.

[97] J. C. Ahn, A. Connell, D. A. Simonetto, C. Hughes, and V. H. Shah, "Application of Artificial Intelligence for the Diagnosis and Treatment of Liver Diseases.," *Hepatology*, vol. 73, no. 6, pp. 2546–2563, Jun. 2021, doi: 10.1002/hep.31603.

[98] Q. Li, J.-F. Li, and X.-R. Mao, "Application of artificial intelligence in liver diseases: From diagnosis to treatment," *Artificial Intelligence in Gastroenterology*, vol. 2, no. 5, pp. 133–140, 2021, doi: 10.35712/aig.v2.i5.133.

[99] S. Luper, "A review of plants used in the treatment of liver disease: part two.," *Altern Med Rev*, vol. 4, no. 3, pp. 178–188, Jun. 1999.

[100] R. Romanelli and C. Stasi, "Recent Advancements in Diagnosis and Therapy of Liver Cirrhosis," *Curr Drug Targets*, vol. 17, Jun. 2016, doi: 10.2174/1389450117666160613101413.

[101] C. Eckard *et al.*, "Prospective histopathologic evaluation of lifestyle modification in nonalcoholic fatty liver disease: a randomized trial.," *Therap Adv Gastroenterol*, vol. 6, no. 4, pp. 249–259, Jul. 2013, doi: 10.1177/1756283X13484078.

[102] N. Chalasani *et al.*, "The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases.," *Hepatology*, vol. 67, no. 1, pp. 328–357, Jan. 2018, doi: 10.1002/hep.29367.

[103] F. Damas, S. Phillips, F. C. Vechin, and C. Ugrinowitsch, "A review of resistance training-induced changes in skeletal muscle protein synthesis and their contribution to hypertrophy.," *Sports Med*, vol. 45, no. 6, pp. 801–807, Jun. 2015, doi: 10.1007/s40279-015-0320-0.

[104] S. Dasarathy and M. Merli, "Sarcopenia from mechanism to diagnosis and treatment in liver disease.," *J Hepatol*, vol. 65, no. 6, pp. 1232–1244, Dec. 2016, doi: 10.1016/j.jhep.2016.07.040.

[105] C. F. Rose, "Ammonia-lowering strategies for the treatment of hepatic encephalopathy.," *Clin Pharmacol Ther*, vol. 92, no. 3, pp. 321–331, Sep. 2012, doi: 10.1038/clpt.2012.112.

[106] A. H. Lockwood, "Blood ammonia levels and hepatic encephalopathy.," *Metab Brain Dis*, vol. 19, no. 3–4, pp. 345–349, Dec. 2004, doi: 10.1023/b:mebr.0000043980.74574.eb.

[107] J.-H. Yan, B.-J. Guan, H.-Y. Gao, and X.-E. Peng, "Omega-3 polyunsaturated fatty acid supplementation and non-alcoholic fatty liver disease: A meta-analysis of randomized controlled trials," *Medicine*, vol. 97, no. 37, 2018, [Online]. Available: https://journals.lww.com/md-

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1767-1783 | ISSN:2251-6727

journal/fulltext/2018/09140/omega_3_polyunsaturated_fatty_acid_supplementation.40.aspx

[108] C.-H. Lee, Y. Fu, S.-J. Yang, and C.-C. Chi, "Effects of Omega-3 Polyunsaturated Fatty Acid Supplementation on Non-Alcoholic Fatty Liver: A Systematic Review and Meta-Analysis.," *Nutrients*, vol. 12, no. 9, Sep. 2020, doi: 10.3390/nu12092769.

[109] N. D. Freedman *et al.*, "Coffee intake is associated with lower rates of liver disease progression in chronic hepatitis C.," *Hepatology*, vol. 50, no. 5, pp. 1360–1369, Nov. 2009, doi: 10.1002/hep.23162.

[110] T. E. Starzl, A. J. Demetris, and D. Van Thiel, "Liver transplantation (1).," *N Engl J Med*, vol. 321, no. 15, pp. 1014–1022, Oct. 1989, doi: 10.1056/NEJM198910123211505.

[111] B. van Hoek, J. de Boer, K. Boudjema, R. Williams, O. Corsmit, and O. T. Terpstra, "Auxiliary versus orthotopic liver transplantation for acute liver failure. EURALT Study Group. European Auxiliary Liver Transplant Registry.," *J Hepatol*, vol. 30, no. 4, pp. 699–705, Apr. 1999, doi: 10.1016/s0168-8278(99)80202-5.