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An Overview of Some Plant Based Products With Hepatoprotective Activity(A review)

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Abstract

In folk medicine there are various medicinal amalgamation possessing hepatoprotective activity. Toxins may cause liver insult as well. Hence, many pharmaceutical companies are targeting herbal medicines for the treatment of liver abnormalities and towards evolving a safe and effective formulation with desired route of administration. Review focused on the studies showing hepatoprotective effect using marine compounds and plant derived compounds. Liver disorder, a global health problem, usually include acute or chronic hepatitis, heptoses, and cirrhosis. It may be due to toxic chemicals and certain antibiotics. Uncontrolled consumption of alcohol also affects liver in an unhealthy way. To cure liver disorders several formulations of medicinal plants are being used. It is observed that hepatoprotective effect of plant is mostly due to flavonoids, alkaloids, terpenoids, steroids, and glycoside. A single drug cannot be useful for all the types of liver disorders. Therefore, several plant extracts for liver illness resulting fromdifferent causes such as poisonous chemicals, viruses, extra alcohol consumption, and repeated administration of medication is to be considered. By using standards of protection and efficacy, manufacture of plant products need to be taken into consideration. Current review provides an understanding of ethnopharmacology and toxicology of several medicinal plants manifesting hepatoprotective potential. Despite of varied database analysis new discoveries and their probabilities, evidences on viral hepatitis treatment and/or liver cirrhosis are inadequate. Further information about phytotherapy, toxicology, quality control studies shall be endorsed. Further in depth studies are required to discover quality trait like structure activity relationship, mechanism of action, safety and toxicity and therapeutic potential of phytoconstituents in clinical settings.

Aim: The phytoconstituents studied for their protective effect in liver diseases are reviewed.

Keywords: Liver disease, Hepatoprotective herbs, Phytoconstituents .

Introduction

The liver is a crucial organ that regulates various functions in the body such as, detoxifying, storage, secretion, and metabolism. Distortion of some of these functions is usually associated with hepatic damage caused by various agents and environmental factors. Most of the hepato-toxic agents act by generating oxidative stress, reactive oxygen species,oxidative damage in proteins, DNA, and reducing ATP. Notably, protecting the liver from hepato-toxic agents and their harmful effects i.e. altering the anti-radical defensive mechanism is called hepatoprotection[(1)]. The persistence of toxins in liver tissue results in liver scarring which is known as fibrosis. This fibrosis results in impaired blood flow in the liver and influences its structure and capacity to function legitimately commonly characterized as called cirrhosis. This condition if remains untreated, causes accumulation of blood in the spleen and the digestive organs to cause portal hypertension including loss of blood and ascites (build-up of fluid in the abdomen)[(2)]. Further, these pathological conditions diminish the liver's capacity to store and process supplements required for survival. Also, the inability of the liver to remove toxins from the bloodstream eventually leads to mental confusion and even coma (hepatic enteropathy) and death. According to WHO reports, liver diseases lead to approximately 2.4 million deaths per year. For instance, over 900 drugs have been accounted as the sole reason for liver injury from which 50% of acute liver failures, 10%cases of acute hepatitis, 5% of hospitalizations, cirrhosis, and chronicliverdisease[(3)]. Despite the presence of several advancements in the modern era, the incidence of the hepatic disease has not reduced and on the contrary, an exponential increase is observed. Numerous plants were studied for their ethno pharmacological activity for liver illnesses. But it is tough to recover the damaged liver from toxicity. Natural products containing active phytoconstituents were significantly used showing the high recovery of liver injuries. Accordingtothe well-searched scientific articles, it is observed that herbal medicines showing liver protectionexerted their activity through properties related to antioxidants[(4)].

Materials and Methods

In this article, several resources were spotted through editorial books, articles, indexed and non-indexed journals. Other databases mainly Google Scholar, Pubmed, Scifinder, Science-direct,

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Medline were used to collect all the pertinent appropriate findings to the literature articles published on hepatoprotective action of medicinal plants. Some books like Charaka Samhita, Sushruta having traditional records of ancient medicines were also exploited. Several common names like hepatitis, lipid peroxidation, hepatoprotective potential, antioxidants, herbal medicines, ethnopharmacology were the search tools. Patents, Conferences proceedings, case reports were not included in the study as from a scientific point of view these were considered unconvincing. Several non-indexed resources were exploited through health websites, international health agency reports. Due focus is given on plants with a descriptive explanation of hepatoprotective potential.Studies like tumor cell lines and tumor-bearing animals have not been considered while doing a literature survey for this article. Extra motivation to prohibit such examinations was conflicted utilization of HCC cell lines for examining both cytotoxic and cytoprotective impacts of tested compounds, bringing about disputable outcomes.

Pathophysiology of Liver

The largest internal organ in the body is liver. It is located below the diaphragm in the upper right quadrant of the abdominal cavity. Its weight is 1.6 kg in men and 1.4 in women. It consists of two lobes. The right lobe is much greater in size than the left lobe. They are again divided into smaller lobules. There are millions of parenchymal cells also known as hepatocytes which are known to be metabolic cells of the liver as shown in figure 1[5].It is highly vascular. From hepatic portal veins, most of its blood supply (around 80%) comes from which delivers the blood with essential nutrients to the small intestine. These huge veins further partition into vessels to provide blood to each one of the lobules[6,7].

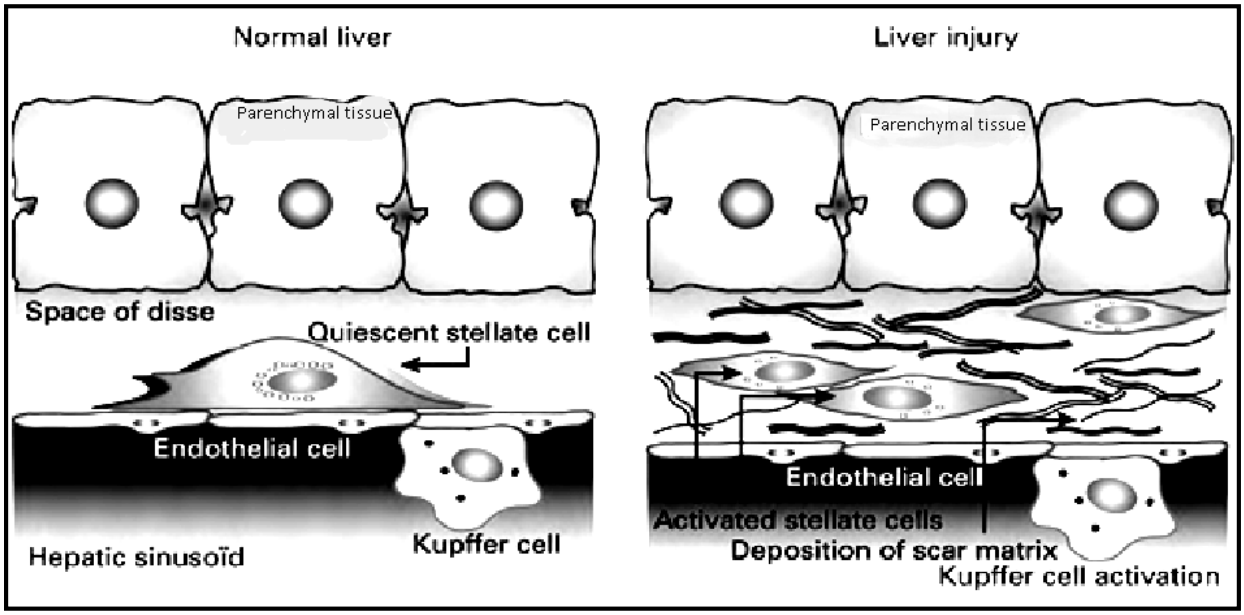

Figure 1. Diagram depicts 4 major liver cell types (parenchymal cells/ hepatocytes, stellate cells, kupffer cells, endothelial cells) in normal liver and in liver injury.

Reasons for hepatic diseases

Viral infections, alcohol consumption, genetic disorders, immunological disorders, non-alcoholic fatty liver disease, excessive medications, malignancy, abnormalities in structures like biliary arteries are very common causes of chronic liver disease.Such conditions are common indicationsforliver transplantation[8, 9].

Oxidants level decrease/ antioxidants level increase

Antioxidants, at moderately low concentrations, can rival other substrates and lead to hinder the oxidation of those substrates[10].It is apparent that few phytoconstituents can instigate microsomal enzymes either by quickening the discharge of the hepatotoxin or by hindrance of lipid peroxidation initiated by it. Saponins, flavonoids, triterpenoids, alkaloids are well- known to have hepatoprotective activities[11]. They are expected to exert their antioxidant activity by scavenging free radicals that leads to lipid peroxidation[12]. There are few enzymes which help in inducing protection from oxidants either by causing neutralization of ROS formation or inhibition like super oxide dismutase, peroxidase, and catalase[12]. CYP's inhibition is known to be cause by terpenoids present in plants as one of the essential phytoconstituents by conjugation mechanism. As major metabolic activities occur in liver hepatic cells, variety of enzymes are involved in it, which include, Aspartate aminotransferase (AST), Alanine transaminase

ALT, Alkaline Phosphatase (ALP). The raised activities of these enzymes lead to hepatic cell damage further causing functional integrity and cellular leakages. There are several agents which harm liver in cellular breakdown process and are known as hepatotoxins, which is associated with raised levels of ALP,ALT, bilirubin, triglycerides, and cholesterol in serum. Hepatotoxins produce changing degrees of harm to the liver[13].

Oxidative degradation of lipids and free radicals

It is reported that free radicals inhibit lipid peroxidation [14]. As there is increase in lipid peroxidation due to ethanol, there are more chances of development of liver cirrhosis. Due to lesser toxicity, plant-based medicines are preferred as hepatoprotective agents. This has lead to increase in the research activities based on hepatoprotective effects of phytoconstituents. According to Hartmut Jaeschke, 2011,livercell death is induced by stress such as ischemia-reperfusion, cholestasis, and drug toxicity. These factors can trigger a sterile inflammatory response with activation of innate immune cells through release of damage-associated molecular patterns (DAMPs). A similar inflammatory response can be induced by pathogen-associated molecular patterns (PAMPs), such as endotoxin. Both DAMPs and PAMPs activate through toll-like receptors the resident macrophages (Kupffer cells) and recruit activated neutrophils and monocytes into the liver. Central to this inflammatory response is promotion of reactive oxygen species (ROS) formation by these phagocytes. ROS are the principal toxic mediators by which inflammatory cells kill their targets, e.g. bacteria during host defense but also hepatocytes and other liver cells. The mechanism of ROS-induced cell killing during inflammation involves the promotion of mitochondrial dysfunction through an intracellular oxidant stress in hepatocytes leading mainly to oncotic necrosis and less apoptosis. Although there is satisfactory progress in interpretation of ROS role, more study is needed to explore the exact mechanism of working of ROS in acute liver inflammation and progress with clinical therapeutic effect that successfully hit the harmful effect due to oxidative stress with intransigency to essential function of reactive oxygen species in host defense.

Liver disease and alcohol

According to Wahid A, alcohol dehydrogenase converts ethanol to acetate that generates ROS via cytochrome P4502E1. This process causes oxidative stress in liver and consequently leads to hepatic damage and disturbs the rigidity of structure of liver cell membranes due to which in blood stream cytosolic enzymes are exuded. Hence, concentration of AST and ALT in mitochondria and blood stream is escalated. Due to this mechanism the bilirubin level in serum also becomes high which in turn causes increase in erythrocyte sedimentation rate[16].

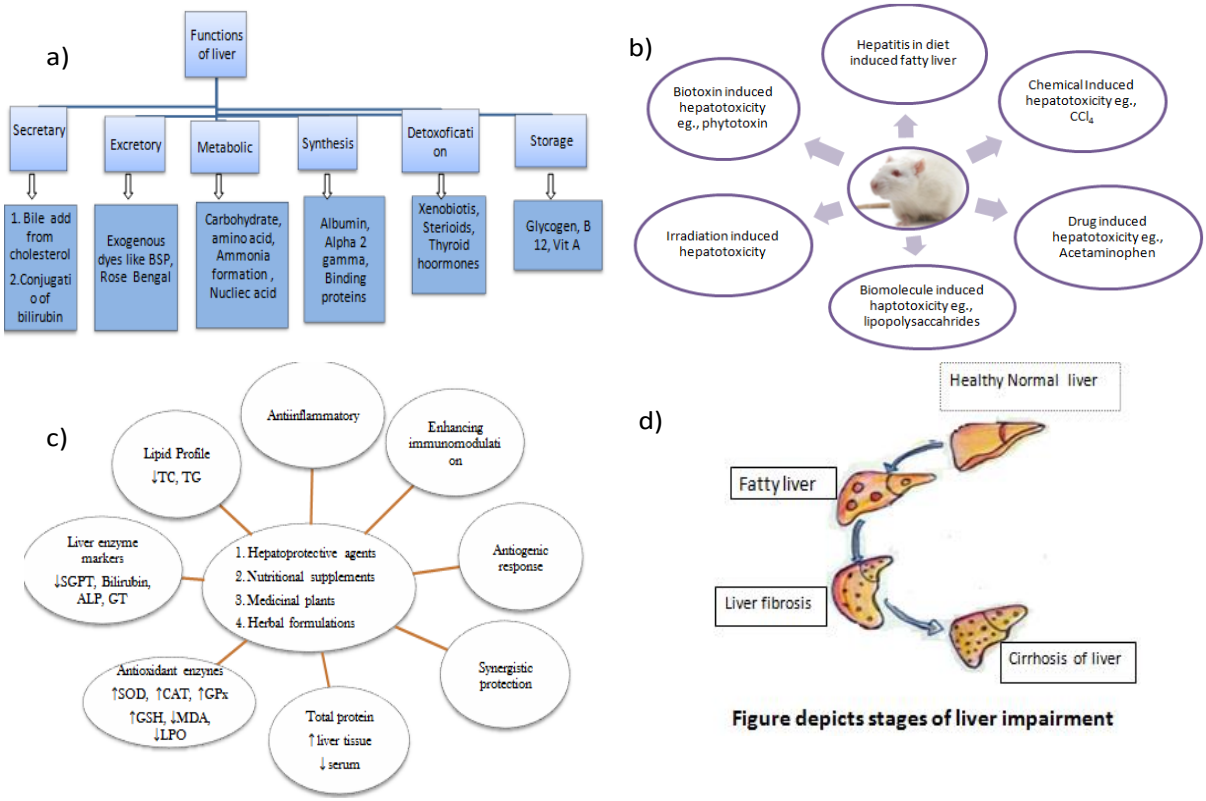

Figure 2. Brief overview of a) Functions of liver, b) In-vivo Studies carried out to understand the

hepatotoxicity, c) Various factor effecting liver health and their effect in change in levels, d) stages of liver impairment.

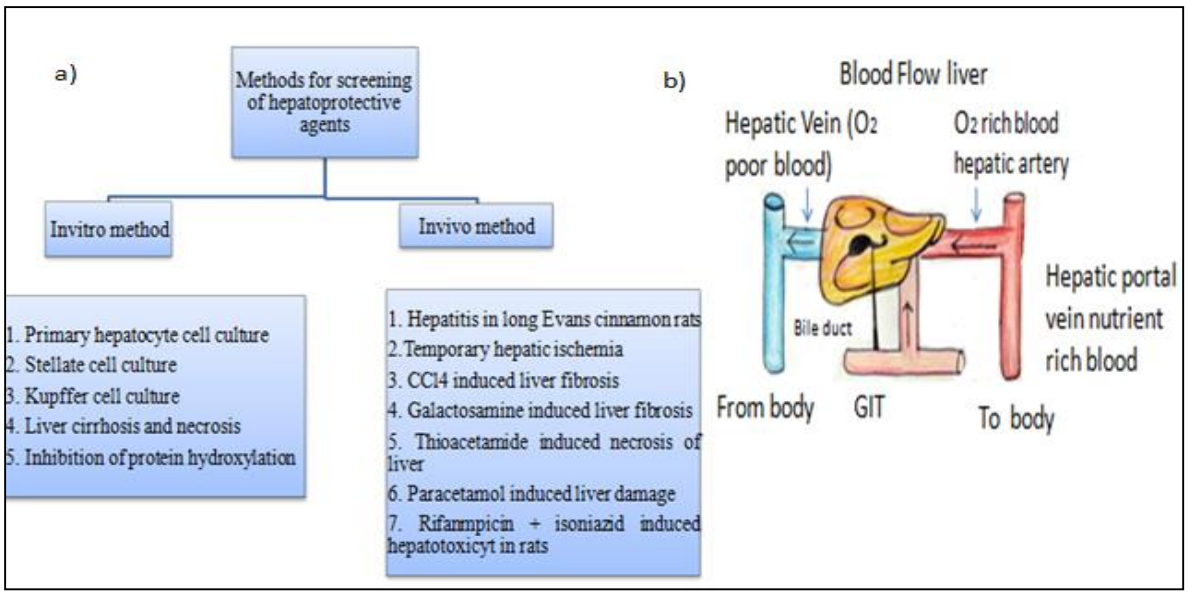

Figure 3. a) Depicts fever methods of screening of hepatoprotective agents, b) Blood flow in liver (from and to body)

Correlation of Growth Factors and Hepatoprotection by the Folk Medicines

Insulin-like growth factor

One of the main factors that contribute to malnutrition in cirrhotic patients is decreased hepatic production of insulin–like growth factor (IGF-I). It has wide range of anabolic activities and is produced under the stimulus of growth hormones located in the hepatocytes [16,8].Studies have revealed the effect of IGF – I on histopathologic changes on liver of rat with CCl4 induced cirrhosis, where free radicals are the prime cause of hepatotoxicity which leads to cell damage. The evolved oxidative stress causes lipid peroxidation, dysfunction of mitochondria and also ATP depletion[8].Antioxidants scavenge the free radicals and can regulate the gene expressions associated with fibrosis, lipogenesis, and inflammation.

Hepatocyte growth factor(HGF)

HGF is also called scatter factor. Regeneration drug injury and liver repair are the two key roles which HGF possesses. It forms a complex network of signaling pathway which activates the cellular redox control, liver survival, and repair function. It happens when HGF binds to c-met receptor after autophoshyrlation which induces varied signal transduction proteins[17].However, more research is need to identify the exact mechanism of intervention in HGF activation of signals and c-met receptors.

Role of phytoconstituents in hepatic disorder

Hepatic disorders are prominently prevalent in India[18].Many allopathic drugs, such as triclabendazole, pembrolizumab etc., are extensively used in the treatment of these liver diseases but they are associated with several adverse effects like abdominal pain, decreased appetite, headache, urticaria, mucoskeletal chest pain etc. Moreover, these medicines are liable to cause socio-economic burden[19].

Due to these concerns, extensive work on alternative medicine is needed. Some herbal plants are also screened for their hepatoprotective potential; however, their synergistic effects have not been studied yet. Moreover, toxicity studies of some plants have not been performed which might be toxic at certain extent. Hence, there is a need to develop some alternative cost effective therapies which can be beneficial in the effective management of severe liver injuries or diseases. The Indian ancient literature mentions various medicinal herbs that may be useful for liver diseases; however, they lack proper validation. Thus, there is a growing need to focus on medicinal plants as hepatoprotective agents and establish their safety as well as efficacy in the treatment of liver diseases. Nature is a storage facility of various restorative herbs containing dynamic bio-active constituents which are considered as potential source of medicines and play a key role in the management of various diseases. A single drug cannot be effective against all types of liver diseases[30]. Notwithstanding the significant approval of several folk medicines conventionally and for liver diseases in particular, they are still unsatisfactory treatment methods to liver diseases. The factors responsible for their occurrences are lack of:

1) Toxicological evaluation
2) Randomized and controlled clinical trials

3) Active ingredient identification
4) Herbal drugs standardization

A large group of folk medicines are reported to show hepatoprotective activities. Various phytoconstituents and plants, within India as well as in other geographical continents, possess liver protecting ability and some of the patented formulations are available in market [60].

Hepatoprotective medicaments

The folk medicines are expected to be safe and not possessing serious adverse response, as they are derived from nature and are effortlessly accessible.

Table 1. Summarized overview of plants along with their botonical names/Family, parts used for their therapeutic effect, Extract studied, inducing agents, histopathological and biochemical parameters showing hepatoprotective activity, Chemical Constituents.

Name of plant (source/Family)	Plants part used	Extract Studied	Hepatotoxic inducing agent	Biochemical and Histopathological parameters studied	Chemical Constituents
Abutilon indicum (Malvaceae) [21]	Whole plant	Aqueous	CCl4, paracetamol	Activates antioxidative enzymes	carbohydrates, glycosides, steroids, tannins, Phenolic compounds and flavonoids
*Acacia catechu (*Leguminosae*)*[22]	Powdered pale catechu	Ethyl acetate	Carbon tetrachloride	SGOT, Bilirubin content, SGPT, SAP	Taxifolin, Quercetin, Catechin, rutin and isorhamnetin
*Adhitoda vasica (*Acanthaceae*)* [23]	Leaves	Aqueous	CCl4	Reduced elevated levels of SGOT,SGPT	alkaloids, tannins, flavonoids, terpenes, sugars, and glycosides
Alchornea cordifolia(Euphorbiaceae) [24]	Leaf	Methanol	CCl4	Decreases ALT, AST value	Steroids, Flavonoids, terpenoids
Allium cepa (Liliaceae)[27]	Bulb extract	Aqueous	Cadmium, Paracetamol, Acetaminophen	SGOT, SGPT, alkaline phosphatase, direct and total bilirubin	carbohydrates, proteins, flavonoids potassium, sodium and phosphorus
Amaranthus spinosus (Amaranthaceae) [25,26]	Whole plant	Ethanol	CCl4	MDA, hydroperoxides, GSH, SOD and CAT	*Alkaloids, flavonoids*
Anogeissus latofilia(Combretaceae) [28]	Bark	Hydroalcoholic	Ethanol, CCl4	Reduces ALT,AST,ALP levels and lipid peroxidation	Tannins, gallic acid, ellagicacd, lutin and quercetin
Apium graveolens (Apiaceae) [27]	Seeds	Methanol, Pet. Ether, Acetone	Paracetamol, Thioacetamide	Reduces raised serum transamina-ses, ALP,total protein and albumin	Flavonoids, anthrons, xanthons, tannins
Arachniode sexilis (Dryopteridacea) [29]	Rhizome	Ethanol	CCl4	Reduces levels of SGPT and SGOT	Polyphenols

Continued table 1.

Name of plant (source/Family)	Plants part used	Extract Studied	Hepatotoxic inducing agent	Biochemical and Histopathological parameters studied	Chemical Constituents
Azadiracta indica(Meliaceae) (30)	Leaves	aqueous, alcoholic, ethyl acetate and petroleum ether	Paracetamol, Carbon tetrachloride	Glutathione peroxidase (GPx), GST, SOD and CAT	Quercetin-3-O-β-D-glucoside (ii) Quercetin-3-O-α L-rhamnoside, (iii) Myricetin – 3-O-rutinoside (iv)Kaempferol-3-O-rutinoside (v) Quercetin-3-O-rutinoside (vi) Kaempferol-3-O-β-D-glucoside
Baliospermum montanum (Euphorbiaceae)(31)	Roots	Alcohol, chloroform extract	Paracetamol	GOT and GPT	Flavonoids, Quercitin
Boerhaavia diffusa(Nyctaginaceae)(32)	Roots	Aqueous	Thioacetamide	Aspartate amino transferase, reduced glutathione levels, AMT, SOD, glutathione peroxidase, catalase and glutathione-S-transferase	alkaloids, flavonoids, steroids, terpinoids, safonine
Butea monosperma Fabacea (33)	flowers	Aqueous	Thioacetamide	Prevents from oxidative potential by inducers	Butein, butin, isobutin, Iso-monospermoside
Byrsocarpus coccineus (Connaraceae) (34)	Leaf	Aqueous	CCl4	Rich in antioxidants and strongly inhibitlipid peroxidation Reduces the AST,ALT,ALP	Flavonoids and Polysaccharides
Cassia fistula Fabacea (35)	Leaves	n-hexane	Paracetamol	Facilitates in lowering the serum transaminases, bilirubiln and LAP	Phenolic compounds, cyaniding B2, biflavonoids, triflavonoids

Continued table 1.

Name of plant (source/Family)	Plants part used	Extract Studied	Hepatotoxic inducing agent	Biochemical and Histopathological parameters studied	Chemical Constituents
Cochlospermumplanchoni(Coclospermaceae)[36]	Rhizomes	Aqueous	CCL_4	Total bilirubin, Alkaline phosphatase and Alanine aminotransferase	Flavonoids, Sterols, Lignans
Cordiama cleodii(*Boraginaceae*) [37]	Leaves	Ethanolic	CCL_4	SGOT, GPT	Flavonoids
Crataeva nurvala (Capparaceae) [38]	Stem Bark	Ethyl acetate	CCl4	Scavenges peroxyl radicals by facilitating the levels of enzymes system which have antioxidant properties	Lupeol, lupeol linoleate
Crossandrainfundibuliformis (Acanthaceae) [39]	Leaf	Pet . Ether	CCl4	Decreases heptocyte peroxidation and lipoprotein lipase in liver	Phytosterols, phenolic compounds, flavonoids
*Curcuma longa (*Zingiberaceae)[40]	Rhizome	Aqueous	CCl4 and TAA	SOD, CAT enzymes	Flavonoids, steroids, tumerone, atlantone, and zingiberene
Cyathea gigantean (Cyatheaceae) [41]	Leaves	Methanol	Paracetamol	Reduces the raised level of SGOT,SGPT,ALP,TB	Triterpenes, sterols, saponins, flavonoids
Daucus carota (Apiaceae) [42]	Seeds	Methanol	Paracetamol, Isoniazid, Alcohol	Decreases SGOT,SGPT,ALP	Flavonoids
Enicostemmaaxillare(Gentianaceae) [43]	Whole plant	Ethanol-water	d-galactosamine, Paracetamol	Decreases the lipid peroxidation	Secoiridoid glycoside
Fumaria indica(Papaveraceae) [44]	Whole plant	Ethanol-water	carbon tetrachloride, paracetamol and rifampicine	Reduces the elevated levels of serum transaminases (SGOT,SGPT)	Narceimin, (-)-tetrahydrocoptisine, bicuculine and fumariline

Continued table 1.

Name of plant (source/Family)	Plants part used	Extract Studied	Hepatotoxic inducing agent	Biochemical and Histopathological parameters studied	Chemical Constituents
Gardenia gummifera(Rubiaceae) [45]	Roots	Methanol	Paracetamol	Su.resses the raised levels of serum ALT AST, MAD ALP, LDH	Phenols, Flavonoids
Ginkgo macrophylla (Ginkgoaceae) [46]	Dried extract	Ethanolic	CCL_4 , lantadenes	SGOT, Serum glutamic pyruvate transaminase, SAP and Bilirubin content	Polyphenols
Glycyrrhiza glabra (Fabaceae) [47]	Powdered form of root	Powdered root mixed with animal feed	Carbon tetrachloride	Lipid peroxidation	triterpene, saponins, glycyrrhizin/glycc yrrhizic acid and glycyrrhetic acid
Graptopetalumpara guayense(Crassulaceae) [48]	Whole plant	Aqueous	Ethanol, CCl4	AST, ALT, LDH, SOD, GPx, catalase AT, and GST	Anthocyanins, Phenolic compounds
Heterothecainuloides (Asteraceae) [49]	Whole plant	Methanol, Acetone	CCl4	Inhibits lipid peroxidation	Stigmasterol, Quercetin, b-Sitosterol, Cadalen-15-oic acid, kaempferol
Hoslundia opposita (Lamiaceae)(50)	Stem	Methanol and ethyl acetate	Carbon tetrachloride	Aspartate amino transferase and Alanine amino transferase and Bilirubin	saponins, alkaloids, tannins, sterols/triterpenes, acidic compounds,
Luminetzeraracemosa(Combretaceae) [51]	Bark	Ethanol, Water	Acetaminophen	CAT, SOD, and GST	Flavonoids, alkaloid, polyphenol
Lycium chinense (Solanaceae) [52]	Fruit	Ethyl acetate	CCl4	Blocked the release of SGPT Free radical scavenging property	Cerebrosides and pyrrole derivatives , flavonoids

Continued table 1 .

Name of plant (source/Family)	Plants part used	Extract Studied	Hepatotoxic inducing agent	Biochemical and Histopathological parameters studied	Chemical Constituents
Mallotus japonicas (Euphorbiaceae)[53]	Whole plant	Water	d-galatosamine	Prevents the elevation of MDA and glutathione content in the liver	Bergenin, Gallic acid, quercetin
Melothria heterophyll(Cucurbitaceae) [54]	Aerial plants	Ethanol	CCl4	AST, ALT, ALP, total bilirubin and protein. In liver homogenate varied antioxidant enzyme activities were studied and Lipid peroxidation product	B-sitosterol,, glycosides, saponin, flavonoids
Moringa oleifera (Moringaceae) [55]	Stem bark	Pet. Ether, CCL4	Cadmium	AST, ALT, ALP, significant ($p \leq 0.01$) increase of LPO and decrease in SOD	Phenolic content and flavonoids
Ocimum sanctum(Lamiaceae)[56]	Whole Plant	Aqueous	paracetamol, CCl4, lead	albumin globulin ratio, serum proteins, APT, histopathology of liver	rosmarinic acid, β caryophyllene, oleanolic acid, eugenol, ursolic acid, carvacrol, germacrene β elemene, linalool,
Phyllanthus niruri(Euphorbiaceae) [57-59]	Leaves and fruits	Methanolic and aqueous	Carbon tetrachloride , Paracetamol	(GPT) Glutamate pyruvate transaminase, Glutamate oxaloacetate transaminase (GOT)	six phenolic compounds; epicatechin, (+)-gallic acid, (-)-epigallocatechin, (-)- gallocatechin, (-)-epigallocatechin 3-O-gallate , epicatechin, 3-O-gallate and (-)-Amariin, lignans

Continued table 1 .

Name of plant (source/Family)	Plants part used	Extract Studied	Hepatotoxic inducing agent	Biochemical and Histopathological parameters studied	Chemical Constituents
Piper longum (Piperaceae) [60]	Fruit	Milk extract	Carbon tetrachloride	SGT, SGPT, Bilirubin	piperine (1-piperoyl piperidine)
Pleurotuseryngii (Pleurotaceae) [61]	Dried fruits	Water	Alloxan, CCl4, thioacetamide, ethanol, diethyl nitrosamine, dimethyl nitrosamine, deltametrin	Increases antioxidant enzymes activities, CAT, SOD, GSH and prevents uncontrolled lipid formation in liver	lipids, Polysaccharides, peptides, dietary fibre and sterols
Scoparia grandiflora(Scorphulariaceae)[62]	Whole plant	Methanol, diethyl ether and petroleum ether	Carbon tetrachloride	Alanine amino transferase (AMT), Total bilirubin and Alkaline phosphatase	Ketones, G-sitoterol, alkaloids, flavanoids, diterpenoids, hexacosonol,
Spirulina platensis (Spirulinaceae) [63]	Spirulina microalgae	-	Lead	n GSH content, and LDH, AChE, SOD, CAT and GST enzymes	vitamins, minerals, carbohydrates, carotenoids, xanthophyll, and γ-linolenic acid
Terminialiacatappa (Combretaceae) [64]	Leaves	Chloroform, Aqueous	CCl4	Prevents the mitochondrial disruption intra-mitochondrial Ca^{+2} overload and su.resses Ca^{+2} ATPase activity	Flavonoids (Keam.ferol, quercitin), tannins (punicalin, punicalagin, tercatin), saponins, phytosterols
Trianthemadecandra (Aizoaceae) [65]	Leaves	Aqueous	CCl_4	Alanine amino transferase, AMT and Bilirubin	flavonoid, fats, terpenes, carbohydrates, tannins, and alkaloids
Trianthemaportulacastrum (Aizoaceae) [66]	Whole plant	Ethanol	Paracetamol, Thioacetamide	Stimulates hepatic regeneration	Saponin and Punarnavine
Tridaxprocumbens (Asteraceae) [67,68]	Leaves	Ethanolic extract	Paracetamol , d-galactosamine	Glutathione, superoxide dismutase and catalase	flavonoids, alkaloids, tannins, carotenoids

Continued table 1 .

Name of plant (source/Family)	Plants part used	Extract Studied	Hepatotoxic inducing agent	Biochemical and Histopathological parameters studied	Chemical Constituents
Trigonella[69]	Leaves	Methanolic	Carbon tetrachloride, deltamethrin	Serum bilirubin level, SGOT, SGPT	polysaccharides, saponins, fibers, Flavonoids and alkaloids like trigonelline, trigocoumarin, choline
Trigonella foenumgraecum (Fabaceae) [70,71]	Seed	Polyphenolic	Thioacetamide	Alkaline phosphatase, γ-glutamyl transferase, Serum gamma glutamyl transferase (GGT), Lipid peroxidation (LPO), Glutathione reductase and peroxidase, Xanthine oxidase (XOD)	Polyphenolic compounds
Tylophora indica(Asclepidaceae) [71]	Leaves	Methanolic	Carbon tetrachloride	SGOT, Serum glutamic pyruvate transaminase, Total Bilirubin	Alkaloids, steroids, saponins, triterpenes, steroids
V. Trifolia (Verbenaceae) [72]	Leaves	Water and ethanol	Carbon tetrachloride	Total protein, AMT, Alanine amino transferase	Flavonoids , triterpenoids

Conclusion

The herbal medicine popularity is being increasing for many decades with regards to liver diseases. Hepatic disorders may be caused by toxic chemicals and certain drugs. Uncontrolled consumption of alcohol also affects liver. Several formulation of medicinal plants are used to cure liver disorders. It is observed that hepatoprotective effect of plant is mostly due to flavonoids, alkaloids, terpenoids, steroids, glycoside. A single drug cannot be useful in position to all types of excessive liver problems. Several plant extracts for liver illness results from poisonous chemicals, viruses, extra alcohol consumption and repeated administration of medication. Well modified and updated metholodologies and clinical trials are needed to study the hepatoprotective mechanism of folk medicines. This approach will lead to several other discoveries which will enable the researchers to

come up with numerous dosage forms in ayurvedic medicine. However,herbal remedies are not well documented and hence are not much prescribed. An attempt has been made in this review article to highlight various mechanism of hepatoprotection of some plants. This article extends a help to the scientists, researchers, and scholars who are working in the therapeutic field to develop a cure for liver diseases.

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Conflict of Interest

The authors have no conflict of interest.

Authors Contribution

S. Labhade wrote initial version of manuscript. S. Desai, S. Sharma and S. Paliwal revised the manuscript. All authors read and approved the final version of manuscript.

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