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PHYTOTHERAPY IN FUNCTIONAL HEPATIC INJURY

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ABSTRACT: Since ancient times, natural products, especially plants have been utilized to treat variety of disorders, and an astounding number of contemporary medications have been created from them. All across the world, liver problems are prevalent. These conditions are only mildly handled traditionally; however, allopathic treatment always makes the situation worse when used to address more severe conditions. The current review offers summaries of plants (44 species from various families) with hepatoprotective qualities that may be discovered in literature sources from various databases and are properly categorized based on the parts utilized. Through the use of experimental animal models, all the plants were examined scientifically for their ability to protect the liver by testing certain parameters, such as liver indicators (AST, ALT, ALP, total protein content, albumin, and bilirubin), as well as through histological analysis, the hepatoprotective action was scientifically demonstrated. From the review, phytoconstituents such flavonoids, glycosides, terpenoids, and alkaloids are primarily responsible for medicinal plants' hepatoprotective properties. It will be useful for the researchers to discover a field of traditional systems of medicine. Professionals will find it useful to learn about the world of conventional medical practice. More research on these plants is necessary to evaluate their effectiveness, safety for use around sensitive organs, and precise mechanisms of action in the treatment of liver disorders.

INTRODUCTION: The liver is a major organ that plays an important role in the metabolism and elimination of xenobiotics from the human body. The liver is responsible for numerous vital tasks in our survival, including blood purification, detoxification, cholesterol control, digestion, and storage. It is involved in practically all metabolic pathways leading to growth, disease resistance, nutrition delivery, energy provision, and reproduction [1]. The liver also manufactures cholesterol, which is responsible for transporting energy-supplying lipids throughout the body.

The liver performs the majority of the processes through several organs such as the skin, mouth and lungs which are considered as human body's biochemical factory. The liver also metabolises the chemicals in the blood stream [2]. Hepatic disease or Liver disease is a term that affects the cells, tissues, various structures, or functions of the liver while

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Liver cell injury is generally caused by various toxic chemicals (certain anti-biotic, chemotherapeutic agents, carbon tetrachloride (CCl4), thioacetamide (TAA) *etc*.), excessive alcohol consumption and microbes is well-stdudied [3]. The available synthetic drugs in the market to treat liver diseases in this condition also increase damage to the liver. Hence, herbal medicines have been used in the treatment of liver diseases for a long time, so the maintenance of a healthy liver is get possible. Natural products may serve as a major source of potentially useful novel compounds for the development of effective therapy to combat a variety of liver issues. The aim of this review is to demonstrate the list of hepatoprotective medicinal herbs.

This review presents a number of hepatoprotective herbal drugs such as Abelmoschus moschatus, *Andrographis paniculata, Anoectochilus formosanus, Ageratum conyzoide, Ardisia solanacea, Arisaema leschenaultia, Azadira chtaindica, Cassia roxburghii, Cassia auriculata, Callicarpa macrophylla, Capparis spinosa, Chenopodium album, Chrysophyllu malbidum,* Clitoriaternatea, *Cocciniagrandis, Flacourtia indica, Foeniculum vulgare, Givotia moluccana, Hibiscus cannabinus, Indigofera tinctoria, Khaya senegalensis, Lannea coromandelica, Lepidium sativum, Nauclea latifolia, Orthosip honstamineu, Prostechea michuacan, Rubia cordifolia, Scutellaria rivularis. Solanum niigrum, Tridex procubance, Picrorrhiza, Punarnava, Liquorcie, Curcuma longa, Eclipta alba, Fumaria officinalis, Phyllanthus amarus, Phyllanthus niruri, Phyllanthus embellica, Asparagus racemosus, Tinospora cordifolia, Vitis vinifera, Piper longum and Ficus carica* has been reviewed. The present review is also aimed at compiling data on promising phytoconstituents from medicinal plants that have been reported in hepatotoxicity models using the modern scientific system.

Risk Factors Which Cause Hepatotoxicity: Hepatotoxicity is known as liver damage, which is caused by the use of some allopathic medication as those used for HIV, cancer, vomiting, stomachache, or fatigue. Treatment often involves changing the medicines which may be causing the hepato-toxicity. In addition, Individual differences, age, gender, alcohol usage, concurrent drug use, previous or underlying liver illness, genetics, and environmental variables are among the risk factors. Antibiotics such as rifampicin, some nonsteroidal anti-inflammatory analgesics (NSAIDs) such as ibuprofen, antiepiletptic drugs such as carbamazepine, and antipsychotics drugs are the pharmaceutical drugs most frequently associated. Furthermore, Hepatotoxicity has been associated with a variety of substances. Galactosamine, alcohol, thioacetamide, d-galactosamine or lipopolysachharide, thioacetamide, carbon tetra chloride, some antitubercular medications and arsenic are other substances that are used to cause liver injury in animal experiments. Several prescription medicines, herbal medicines, and natural chemical moieties cause hepatotoxicity [4]. In fact, these are the most frequent reasons for a medication to be taken off the market. Acetaminophen is also another example of hepato-toxicity because of the body is not able to get rid of the drug before it begins to cause the damage [5].

Mechanisms of Drug Induced Hepatotoxicity: The processes by which medicines produce hepatotoxicity are mediated by the hepatocytes, cholangiocytes, Kupffer cells, ductal, and epithelial cells. These cells have direct impacts on cell structrures like the mitochondria (Power house of cell), endoplasmic reticulum, cytoskeleton, microtubules, or nucleus of cell. Due to the creation of poisonous or reactive compounds such electrophilic chemicals or free radicals which can lead to a variety of chemical processes, the drug metabolites produced in the liver through biotransformation might induce hepatic injury. That may cause apoptosis, necrosis, or both [6].

Sign and Symptoms of Drug Induced Hepatotoxicity: Hepatotoxicity caused by the intake of commonly used drugs can be difficult to diagnose due to the vast number of symptoms the patient may experience. Hence, it is important to get a medical history report while consuming any medication. The first outward symptoms of hepatitis include yellowing of the eyes and vomiting yellowish fluid. Hepatotoxicity can be as mild as a change in liver function tests presenting no viable symptoms in the patient, to full blown hepatotoxicity and liver failure. If the problem is diagnosed earlier, the greater chances of survival for the patient. Many drugs present the symptoms

of rash, fever and an increase in eosinophils in the blood when ALT levels are increased (this happens in about 30% of cases). The symptoms usually occur within 4 weeks of starting a drug and can seize 8 weeks. The treatment for each different hepatotoxicity case can vary as well, but the first and best solution is to discontinue the drug that is causing the liver damage. Often, times this will eliminate the symptoms, but there are times where the damage is too extensive or an antidote to a particular drug may be administered. Treatment is then varied on an individual basis [7].

Plants used as Hepatoprotective Remedies in Traditional Indian Medicine: All plants in the universe playa pivotal role because they contain medicinal characteristics. Natural remedies for the treatment of liver problems have a long history. Medicinal plants and their derivatives are being employed in some form or another all over the world for healing and wellbeing. Scientific analysis of plants has frequently revealer that active components in these plants are response le for medicinal efficacy. There are many plants but no specific novel approach has been identified to treat liver ailments. Some factors that contribute to this eventuality are (i) Lack of standardization and validation of the natural drugs; (ii) Lack of identification of active phytoconstituents); (iii) Very less amount of randomized controlled clinical trials (RCTs) [8].

The current review examines many types of medicinal plants with the hepatoprotective nature of 44 plants and its significance with its scientific evidence. These herbal medications have demonstrated the potential to preserve normal liver function with or without fewer negative effects. A large number of medicinal plants are found to contain active principles with curative properties against a variety of diseases. A large number of plants and formulations have been claimed to have hepatoprotective activity [9]. The present review is aimed at compiling data based on scientific work on promising active constituents from medicinal plants that have been tested and have significant hepatoprotective activity.

Abelmoschus moschatus: The *Abelmoschus moschatus (AM)* (family *Malvaceae*) is cultivated throughout India. *Abelmoschus moschatus* seed aqueous and ethanolic extract 300mg/kg showed the significant result in the paracetamol induced hepatotoxicity as the value of SGOT, SGPT, ALP and TB, were found significant compared with paracetamol treated animals. The ethanolic extract of AM was found more significant than the aqueous extract [10].

***Andrographis paniculata*:** Andrographolide, an active constituent of *Andrographis paniculata (*Family of *Acanthaceae*) prevented the toxic effects of paracetamol on certain enzymes (SGOT, SGPT and ALP) in serum as well as in isolated hepatic cells. Neoandrographolide increased GSH, glutathione 5-transferase, glutathione peroxidase, SOD and LPO levels. Oral administration of A. paniculata exhibited significant dose dependent activity against paracetamol induced hepatotoxicity. The activity has been measured by levels of serum marker enzymes such as serum glutamate pyruvate transaminase (GPT), serum glutamate oxaloacetate transaminase (GOT), alkaline phosphatase (ALP), and bilirubin in peripheral blood serum, higher levels of lipid peroxides (LPO) and reduction of superoxide dismutase (SOD), catalase, reduced glutathione (GSH) and glutathione peroxidase (GPx) in liver tissue [11].

***Anoectochilus formosanus*:** Aqueous Extracts (AFEW-2) of fresh whole plant of *Anoectochilus formosanus* (Family: Orchidaceae) at dose 130 mg/kg showed inhibition of chronic hepatitis (induced by CCl4) inmicebyreducing SGPT and hepatic hydroxyproline level. It also decreased the hypoalbuminemia and splenomegaly. In an *in-vitro* study, the LD_{50} values for H_2O_2 induced cytotoxicity in normal liver cells were significantly higher when treated with kinsenoside (isolatedfromAFEW-2) pretreatment at the dose of 20-40ug/ml. Methanolic extract (100 and 300 mg/kg) and water extract (300 and 500 mg/kg) of *A formosanus* enhanced the recovery of liver injury [12].

***Ageratum conyzoide*:** The methanolic extract of aerial parts of *Ageratum conyzoides* was used for evaluation of the hepatoprotective activity against CCl4 induced hepatotocxicityin wsitar albino rats at the doses of 200 and 400mg/kg with standard drug silymarin (100mg/kg,p.o).

The hepatoprotective activity was assessed using various biochemical parameters like SGOT, SGPT, ALP, γ-GT, TP and total bilirubin along with histopathological studies were observed after 36hr of CCl4 treatment and the methanolic extract showed significant protection against CCL4 induced hepatocellular injury [13].

***Ardisia solanacea*:** The hepatoprotective activity was investigated with alcoholic extract of *Ardisia solanacea* leaves against carbon tetrachloride induced hepatotoxicity. Changes in the levels of biochemical markers to measure hepatic damage like SGOT, SGPT, ALP, Billirubin and Protein were tested in both CCl4 treated and untreated groups. CCl4 (1ml) has enhanced the SGOT, SGPT, ALP and Total Billirubin while total protein level was decreased in the liver. Treatment of alcoholic extract of *Ardisia solanacea* (200mg/kg) has brought back the altered levels of biochemical markers to the near normal levels in the dose dependent manner [14].

***Arisaema leschenaultia*:** *Arisaema leschenaultii belongs to the Family Araceae* and it is commonly known as Dhei or Cobra Lilly. The hepatoprotective potential was observed in the ethanolic extract of *Arisaema leschenaultii blume* tuber against experimentally induced hepatoxicity models in swiss albino mice. Silymarine was given as a reference standard. The ethanolic extract of tuber of *Arisaema leschenaultia blume* had shown very significant hepatoprotection against paracetamol induced hepatotoxicity in swiss albino mice [15].

Azadirachta indica: The effect of *Azadirachta indica* leaf (Family-*Meliaceae*) extract was studied. Serum enzyme levels (glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acid phosphatase and alkaline phosphatase) were elevated by paracetamol in rats was studied with a view to observing any possible hepatoprotective effect of this plant. It is demonstrated that the extract treated group was protected from hepatic cell damage caused by paracetamol induction. The findings were further confirmed by histopathological study of liver [16].

Cassia roxburghii: Seeds of *Cassia roxburghii* DC (Family-*Fabaceae)* had been used as ethnomedicine for various liver ailments for its hepatoprotective activity. The methanolic extract of *Cassia roxburghii* reversed the hepatotoxicity produced by ethanol CCl4 combination in dose dependent manner. The extract at the doses of 250 mg/kg and 500 mg/kg are comparable to the effect produced by standard Liv-52®,a well-established plant drug based hepatoprotective formulation against hepatotoxins [17].

Cassia auriculata: It is commonly known as tanner's cassia, a shrub belongs to the family named *Caesalpiniaceae.* The aqueous (100 mg/kg), methanolic (100 mg/kg) and petroleum ether (50 mg/kg) extracts of the flowers of *Cassia auriculata Linn* were studied for their hepatoprotective activity against paracetamol induced hepatotoxicity in albino rats.

The degree of protection was measured by using various biochemical parameters like serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvate transaminase (SGPT), alkaline phosphatase (ALP), direct bilirubin and total bilirubin. The histopathological studies were also conducted. The aqueous and methanolic extracts of the flowers showed a significant hepato protective activity comparable with those of the standard (Silymarin) [18].

Callicarpa macrophylla: The plant belongs to the Family Verbenaceae. The hepatoprotective activity of the aqueous alcoholic (60%) extract of the aerial parts of *Callicarpa macrophylla (Verbenaceae)* was measured against Paracetamol and carbon tetrachloride induced hepatotoxicity. (Silymarin 25 mg/kg was used as a reference drug, Animals were treated with hydro-alcoholic extract of aerial parts of *C. macrophylla* significantly ($p < 0.05$) reduced the levels of SGOT in serum which is an indicative of hepatoprotective activity. Hydro-alcoholic extract of plant *C. macrophylla* showed significant hepatoprotective property which was evident by biochemical parameters and histopathological reports [19].

Capparis spinosa: *Capparis spinosa (CS)* is a plant belonging to *Capparidaceae* family. Protective action of C. spinosa ethanolic root bark extract was studied in an animal model of hepatotoxicity, which was induced by carbon tetrachloride.

The parameters studied were alanine transaminase and aspartate transaminase levels and duration of sleep. The hepatoprotective activity was also measured by histopathological studies of liver tissue. The levels of serum enzyme were increased which reflecting the liver injury caused by CCl_4. The results demonstrated that the ethanolic root bark extract of *C. spinosa* indicated significant dose-dependent protection against CCl4 induced hepatocellular injury [20].

Chenopodium album: Hepatoprotective activity of dried whole plant of *Chenopodium album Linn,* in acetone and methanol solvent mixture extracts, (in1:1 ratio) against paracetamol induced hepatic injury was studied. Hepatic injury was achieved by injecting 2.5ml/kg of paracetamol in equal proportion with dimethysulfoxide (DMSO) through oral route.

Acetone and Methanolic extract at dose levels of 200 and 400 mg/kg offered significant ($P<0.001$) changes. Hepatoprotective action was supported by reducing the serum marker enzymes like serum glutamate oxaloacetate (SGOT), serum glutamate transaminase (SGPT). They have also reduced the elevated level of serum alkaline phosphatase (ALP), serum acid phosphatase (ACP) and serum bilirubin. Histopathological studies were also carried out. The result obtained were compared with silymarin (100mg/kg; oral), the standard drug [21].

Chrysophyllum albidum: *Chrysophyllum albidum G*. belongs to the *Sapotaceae* family. The leaf extract of *Chrysophyllum albidum* was studied for hepatoprotective activity against rats with induced liver injury by carbon tetrachloride (CCl_4). The results showed that the levels of AST, ALT, ALP and total bilirubin were significantly higher in rats treated with CCl_4 indicating liver injury, while these parameters were decreased significantly ($p < 0.05$) after treatment of rats with the extract. The hepatoprotective potential of *C. albidum* was also evidenced by histopathological studies of liver tissue. The liver tissue of rats in the group treated with CCl_4 showed marked centrilobular fatty degeneration and necrosis while the groups treated with plant extract found signs of protection against this toxicant as evidenced by the absence of necrosis [22].

Clitoria ternatea: *Clitoria ternatea* belongs to the Family- *Leguminoceae.* The hepatoprotective effect against paracetamol-induced liver toxicity in mice with the methanolic extract of *C. ternatea* leaf was measured by obseerving the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and billirubin along with histopathological analysis. The results of the paracetamol-induced liver toxicity experiments showed that mice treated with the ME of *C. ternatea* leaf (200 mg/kg) showed a significant decrease in *ALT*, AST, and bilirubin levels, which were more elevated in the paracetamol group ($p < 0.01$). *C. ternatea* leaf extract therapy also showed protective effects against histopathological alterations. *C. ternatea* leaf extract was found to be effective against the hepatotoxicant, paracetamol [23].

Coccinia grandis: Alcoholic extract of the fruits of *Coccinia grandis* Linn (Family: *Cucurbitaceae*) was measured in CCl4 induced hepatotoxicity in rats and AST, ALT, ALP levels, total proteins, total and direct bilirubin were evaluated. At a dose level of 250 mg/kg, the alcoholic extract significantly ($p<0.05$) reduced the activities of serum enzymes (AST, ALT and ALP) and bilirubin which were comparable to silymarin revealing its hepatoprotective effect [24].

Flacourtia indica: The extracts of the aerial parts of *Flacourtia indica* (Family: *Salicaceae)* were showed the signifcant hepatoprotective properties. The most significant reduction of the serum level of AST and ALT were exhibited by petroleum ether and ethyl acetate extracts. Histopathological examination indicated good recovery of paracetamol induced necrosis by petroleum ether and ethyl acetate extracts. The hepatoprotective effect was exhibited by petroleum ether and ethyl acetate extract through the inhibition of microsomal drug metabolizing enzymes. But, in this study the dose they have used is too high and it is not successful or rationale for human dose [25].

Foeniculum vulgare: *Foeniculum vulgare Mill.* (Family: *Umbelliferae)* is an annual, biennial or perennial aromatic herb. Hepatoprotective activity of Foeniculum vulgare (fennel) essential oil was measured using a carbon tetrachloride induced liver fibrosis model in rats. The hepatotoxicity produced by chronic carbon tetrachloride administration was

inhibited by *Foeniculum vulgare* essential oil with evidence of decreased levels of serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and bilirubin [26].

Givotia moluccana: The *Givotia moluccana* is belongs to *Euphorbiaceae* family. The hepatoprotective activity of aqueous ethanolic extract of aerial parts of *Givotia moluccana* L. was measured in wistar rats using the popular inducing agent carbon tetrachloride (0.1 ml/kg) in 1% olive oil and silymarin (20 mg/kg, p.o.) was used as reference standard. The effect was estimated by measuring the enzymatic levels. This was evidenced by marked reduction in marker enzymes in the serum [27].

Hibiscus cannabinus: In this study the hepaatoprotective activity of a daily oral dose (1.6g kg-1) of aqueous leaf extract of *H. cannabinus* was carried out in albino rats. Liver damage in rats was induced using carbon tetrachloride and paracetamol. The aqueous leaf extract of *H. cannabinus* exhibited a significant ($p<0.05$) hepatoprotective activity against this damage in lowering the plasma transaminases and bilirubin concentration significantly ($p<0.05$) absents of necrosis in liver cells of rats pretreated with extract indicated a protective effect. The extract also inhibited lipid peroxidation, suggesting a possible mechanism of action [28].

Indigofera tinctoria: A bioactive fraction, indigtone (12.5- 100mg/kg) was obtained by fractionation of a petroleum ether extract of the aerial parts of plant *Indigofera tinctoria* (Family-*Fabaceae),* exhibited significant dose dependent hepatoprotective activity against paracetamol (200mg/kg i.p) and CCl_4 (0.5ml/kg p.o mixed with liquid paraffin 1:1) induced liver injury in rats and mice. Pre and post treatment reduced levels of transaminases, bilirubin, TG, LPO and restored the depleted GSH in serum [29].

Khaya senegalensis: The hepatoprotective effect was tested in rats against carbon tetrachloride (CCl_4) induced toxicity. Methanolic extract of the bark of *Khaya senegalensis* showed a hepatoprotective effects against CCl_4- induced hepatotoxicity, which was evidenced by the significant reduction in level of ALT, AST and ALP. The methanolic extract of the bark of Khaya senegalensis possessed strong hepatoprotective effect and protects liver against oxidative damages [30].

Lannea coromandelica: *Lannea coromandelica Houtt. Merrill. (Anacardiaceae)* bark & leaves are used for the study. Hepatoprotective activity of *Lannea coromandelica bark extract (LCBE)* at different doses (400 and 200 mg/kg) was measured on thioacetamide induced hepatotoxicity in rats. Serum bilurubin, cholesterol, sugar and LDH content were altered with the treatments but showed higher with the only ethanolic extract at dose of 400 mg/kg. The hepatoprotective activity of the alcoholic bark extract of *L. coromandelica* might be due to the presence of phenolic groups, terpenoids and alkaloids [31].

Lepidium sativum: The role hepatoprotective of methanolic extract of *Lepidium sativum* (Family *Brassicaceae)* at a dose of 200 and 400 mg/kg was measured in CCl_4 induced liver damage in rats. Significant reduction in all biochemical parameters were showed in groups treated with *Lepidium sativum.* The severe fatty changes in the livers of rats caused by CCl_4 were insignificant in the *Lepidium sativum* treated groups [32].

Nauclea latifolia: Hepatoprotective effect of the ethanol extract of *Nauclea latifolia (NL)* leaf was measured in Wistar albino rats model by applying Acetaminophen as the toxicity inducer and silymarin was used as the standard drug. Levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were increased and the levels of total protein and albumin were decreased in the treated rats. NL leaf extract at (400 mg/kg, bw) dose decreased the elevated levels of the transaminases and restored the normalcy of total protein (TP) and albumin significantly. The activities of catalase (CAT), glutathione Peroxidase (GPx) and superoxide dismutase (SOD) were reduced in hepatotoxic rats but administration with NL leaf extract increased the levels of these enzymes. Histopathological studies showed the restoration of Acetaminophen induced liver damaged with NL administration. From this study it can be concluded that the NL leaf showed significant hepatoprotective action [33].

Orthosiphon stamineus: The hepatoprotective activity of the methanol extract of *Orthosiphon stamineus* (Family- *Lamiaceae*) was assessed in paracetamol induced hepatotoxicity rat model. Change in the levels of biochemical markers such as AST, ALT, ALP and lipid peroxides were assayed in both paracetamol treated and control (untreated) groups. Treatment with the methanolic extract of *Orthosiphon stamineus* leaves (200 mg/kg) has accelerated thereturn of the altered levels of biochemical markers to the near normal profile in the dose dependant manner [34].

Prostechea michuacana: Methanol, hexane and chloroform extracts of *Prostechea michuacana* were investigated against CCl_4 induced hepatic injury in albino rats. The degree of protection was measured by monitoring the blood biochemical profiles. These results showed that methanolic extract of *Prostechea michuacana* could protect paracetamol induced lipid peroxidetion thereby eliminating the deleterious effects of toxic metabolites of paracetamol. The study revealed that the methanolic extract of *Prostechea michuacana* can be a potential herb as hepatoprotective agent [35].

Rubia cordifolia: Rubiadin was isolated from *Rubia cordifolia* Linn, (Family- *Rubiaceae*) and administered to rats in a dose of 50, 100 and 200 mg/kg for 14 days. The substantially elevated serum enzymatic activities of serum GOT, GPT, ALP and GGT; decreased activities of glutathione S- transferase and glutathione reductase were restored towards normalization in dose dependent manner which were induced by CCl_4 treatment in rats. It also significantly prevented the elevation of hepatic MDA formation and depletion of reduced GSH content in the liver [36].

Scutellaria rivularis: Baicalein, Baicalin and Wogonin were isolated from the entire plant of *Scutellaria rivularis* Benth (Family *Labiatae*); Wogonin (5 mg/kg i.p), exhibited best effect in CCl4 and D- GalN treated rats. Baicalein and Baicalin at the dose 20 mg/kg in D-GalN and APAP at dose 10 mg/kg in CCl4 treated rats exhibited significant protection. Protective effects were found by comparing the serum GOT, GPT and histopathologic examination (hepatic lesions) [37].

Solanum nigrum: The effects of *Solanum nigrum* (Family- *Solanaceae*) extract (SNE) was evaluated on thioacetamide (TAA) induced liver fibrosis in mice. SNE decreased the hepatic hydroxyproline and α- smooth muscle actin protein levels in TAA treated mice. SNE inhibited TAA induced collagen (α1) (I), transforming growth factor-β1 (TGF-β1) and mRNA levels in the liver. Histological examination also confirmed that SNE decreased the degree of fibrosis caused by TAA treatment [38].

TABLE 1: REPRESENTS PLANTS WITH DIFFERENT TOXICANTS USED TO PRODUCE LIVER DAMAGE AND SCIENTIFICALLY PROVEN ITS HEPATOPROTECTIVE POTENTIAL

Sr. no.	Scientific Name	Family	Part used	Dose	Toxicant
1	*Tridax procumbens* [39]	Asteraceae	Aerialparts	300mg/kg	D-galectosamine
2	*Picrorrhiza*[40]	Scrophulariaceae	Rhizomes	200 mg/kg	D-galectosamine
3	*Punarnav*[41]	Nytaginaeae	Roots	2 ml/kg	Alcohol
4	*Liquorcie*[42]	Leguminosae	Rhizomes	200-400 mg/kg	Carbon tetraChloride
5	*Curcumalonga*[43]	Zingiberaceae	Rhizome	100-200 mg/kg	Paracetamol
6	*Eclipta alba*[44]	Asteraceae	Leaves, flower	200-400mg/kg	Carbon tetrachloride
7	*Fumaria officinalis*[45]	Fumariaceae	Wholeplant	200-500 mg/kg	Carbon tetrachloride
8	*Phyllanthusamarus*[46]	Euphorbiaceae	Whole plant Exceptroot	100-300 mg/kg	Aflatoxin- B1
9	*Phyllanthusniruri*[47]	Euphorbiaceae	Wholeplant	100 mg/Kg	Carbon tetrachloride
10	*Phyllanthusembellica*[48]	Euphorbiaceae	Fruits	1.8g/kg, 3.6 g/kg	Carbon tetrachloride
11	Asparagus Racemosus[49]	Liliaceae	Roots	Crude hydroalcoholic extract	Carbon tetrachloride
12	*Tinosporacordifolia*[50]	Mennispermaceae	Wholeplant	100 mg, 200 mg and 400 /Kg	Carbon tetrachloride
13	*Vitis vinifera* [51]	Vitacear	roots	100 – 200 mg/kg	Carbon tetra chloride
14	*Piper longum*[52]	Piperaceae	Fruits and roots	300 mg/kg	Carbon tetra chloride
15	*Ficus Carica*[53]	Moraceae	Leaves	50, 100 and 200 mg/lg	Carbon Tetra chloride

Responsible Phytoconstituents for Hepato-protective Activity: Liver protective plants contain a variety of chemical moieties like phenols, Coumarins, Lignans, essential oil, monoterpenes, carotinoids, glycosides, flavonoids, organic acids, lipids and alkaloids. Therefore a plethora of herbs and formulations have been claimed for its hepatoprotective potential so the development of natural hepato protective products has been given a higher importance across the market [54].

Phenolic Compounds: A phenolic compound from two Arnica species has revealed its protective behavior against CCl4 induced toxic symptoms in rats. Umbelliferone, methyl umbelliferone and esculatain have some potential to prevent hepatic damage. The presence of a hydroxyl or ether group at C-6 in these derivatives caused no marked changes in activity. The compounds with a hydroxyl group at C-7 exerted high activity and methylation of C-7 hydroxyl group diminished the activity [55].

Lignans: Lignans Silymarin obtained from the seeds of *Silybrun marianum* (compositae) is the most thoroughly investigated. Silymarin exhibited antihepato toxic activity. Silymarin is a mixture of isomeric flavolignans- silybin, silydianin and silychristen[59].

A series of lignans have been isolated from well-known Chinese traditional drugs Schizandra Chinensis and *S. spheranthera* (Magnoliaceae). These are dibenzo cyclooctane derivatives and include schizandrins, schizantherins, wuweizins and gomisins [56].

Essential Oil: The secretion of the lipid complex was boosted by dill oil and rose oil from various species of the Rosaceae family (Rosaceae). Dill oil was produced from the fruits of *Anethum graveolens* (umbelliferae). Rats were significantly choleretic when exposed to the essential oils from *Perovskia abrotanoids, Salvia rhytidea, Ziziphro afghanica,* and *Origanum glaucum,* which are all members of the Labiatae family. Oils of *Pimpinetta anisum, Foenuculum vulgdre, Apium graveolens,* and *Petroselinum sativam*, all members of the family Umbelliferae, were injected intravenously to greatly accelerate liver regeneration [57].

Terpenoids: Monoterpenoids like (+) Borneol, a bicyclic monoterpenoid, or its esters with fatty acids of dicarboxylic acids, Sesquiterpenoids such as atractylon, β-eudemol and hinesol, Diterpenoids such as Andrographolide and Triterpenoids named as Papyriogenin A, Papyriogenin B, Papyriogenin C, Propapyriogenin A, 11-dehydro propapyriogenin A, 16- episkogenin C and propapyriogenin exhibited hepatoprotective activity. Carotenoids Crocin and crocetin isolated from the fruits of *Gardenia florida* (Rubiaceae), when administered into rabbits, increased the bile secretion [58].

Glycosides: Picroside I and Picroside II, two iridoid glycosides from Picorrhiza kurroa (Scrophulariaceae), have demonstrated a notable liver protective effect in CCl_4-intoxicated rats. Both the seeds of *Piantago asiatica* (Plantaginaceae) and the fruits of *Gardenia jasminoids* (Rubiaceae) contained choleretic geniposidic acid aclycones. *Plantago asiatica* seeds and leaves both contained acubin and iridoid glycoside, which had strong liver- protective properties [59].

Saponins: The effects on liver functions of saikosaponin D and saikosamponin A from B. falcatum are intriguing. Ginseng (Arleaceae) and *Dianthus superbus* (Caryophyllaceae) were found to have gypsogenic series saponins that were efficient at lowering high SGOT and SGPT levels in CCl4-intoxicated rabbits [60].

Flavonoids: A series of experimental investigations made the way for the discovery of catechin type drugs. Flavonoid chemicals are substances that are obtained from plants in nature and are present in various plant components. Vegetables utilise flavonoids in order to thrive and protect themselves from plaques. They are members of a group of phenolic compounds with low molecular weight that are found in a variety of plants [61-62].

Nitrogenous Compounds Alkaloids: Isoquinoline alkaloid from boldine Peumus boldus (Monimlaceae), Protopine from Fumeria, Berberine from Beriberis vulgaris,Indole alakaloid reserpine from Rauwolfia and Pilocarpine from Aristoclochia clementis are the herbs which has significant hepatoprotective activity [63-64].

CONCLUSION: Hepatotoxicity is a prime concern for patients as well as doctors, research scholars and drug development companies. However researchers differentiated several mechanisms and also the analyzing the factors that might be used in diagnosis of liver diseases. This paper demonstrates compilation of herbs having hepatoprotective potential and the underlying responsible phytoconstitients for hepatoprotection using medicinal plants and Professionals will find it useful to learn about the world of conventional medical practises. More research on these plants is necessary to evaluate their effectiveness, safety for use around sensitive organs, and precise mechanism of action in the treatment of liver disorders. This approach will help exploring the real therapeutic value of these natural herbs and standardized or validating the dosage regimen on evidence based findings.

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