World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Published by Atom and Cell Publishers
Available online at: http://www.wjpsonline.org/
Review Article

Medicinal plants are used as a hepatoprotective agents

Mohammad Z[1]*, Zeeshan A[1], Md Wasim H[1], Anayatullah[2], Sahar I, Nazma K[2], Prashant S[2], Shahla P[2]

[1]Department of Pharmaceutics and [2]Department of Pharmacology, Faculty of Pharmacy, Integral University, Dasauli, Kursi Road, Lucknow-226026, India

Received: 19-02-2017 / Revised: 18-03-2017 / Accepted: 29-03-2017 / Published: 30-03-2017

ABSTRACT

Liver is one of the main organs in human body and the chief site for powerful metabolism and Excretion. Thus it's have a surprising role in the maintenance, performance and regulating homeostasis of the body. It is concerned with about all the biochemical pathways to growth, fight. Liver diseases are a chief problem worldwide; viral hepatitis, alcohol, malnutrition, autoimmune and drugs being most critical causes level. The scientific basis for the statement that plants and their active constituents play an important role in the prevention of diseases is continuously advancing. Herbal drugs are becoming more popular in the modern world for their application to cure variety of diseases with less toxic effects and better therapeutic effects. However some limitations of herbal extracts/ plant actives like instability in highly acidic pH, liver metabolism etc. led to drug levels below therapeutic concentration in the blood resulting in less or no therapeutic effect in this review some of the plants with their phytoconstituents studied for protective effect in liver diseases are reviewed.

Key words- Liver diseases, Hepatoprotective plants, Liver metabolism

INTRODUCTION

The liver is the largest glandular organ in the body, and it has more functions than any other human organ. A person's entire blood supply passes through the liver several times a day. The Liver has a pivotal role in human metabolism. Liver produces and secretes bile, it also produces prothrombin and fibrinogen, both blood- clotting factors, and heparin, a mucopoly saccharide sulphuric acid ester that helps keeps blood from clotting within the circulatory system. The liver converts sugar into glycogen Liver involve with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction [1]. The major functions of the liver protein and fat metabolism, detoxification, secretion of bile and storage of vitamin. It maintains healthy liver is a crucial factor for overall health and well beaming [2]. Liver diseases have become one of the major causes of morbidity and mortality in man and animals all over globe and hepatotoxicity due to drugs appears to be the most common contributing factor. About 20,000 deaths found every year due to liver disorders [1]. Many of the modern drugs mainly based on synthetic chemical compounds however have been found to have harmful .side effects in human body [3].Since ancient times, mankind has made use of plants in the treatment of various ailments because their toxicity factors appear to have lower side effects[2]. Many of the currently available drugs 4were derived either directly or indirectly from medicinal plants. Recent interest in natural therapies and alternative medicines has made researchers pay attention to traditional herbal medicine. In the past decade, attention has been cantered on scientific evaluation of traditional drugs with plant origin for the treatment of various diseases. Due to their effectiveness, with presumably minimal side effects in terms of treatment as well as relatively low costs, herbal drugs are widely prescribed, even when their biologically active constituents are not fully identified [3]. The Indian Traditional Medicine like Ayurveda, Siddha and Unani are predominantly based on the use of plant materials. The association of medical plants with other plants in their habitat also influences their medicinal values in some cases. One of the important and well documented uses of plant products is their use as hepatoprotective agents. Hence, there is an ever increasing need for safe hepatoprotective agent [2,4]. Several Indian medicinal plants have been extensively used in the Indian traditional system of medicine for the management of liver disorder. The

***Corresponding Author Address:** Mohammad Zishan, Research Scholar, Faculty of Pharmacy, Integral University, Dasauli, Kursi Road, Lucknow, 226026, E-mail: zishanquadri786@gmail.com*

use of natural remedies for the treatment a large number of medicinal plants have been tested and found to contain active principles with curative properties against a variety of diseases [5]. Liver protective plants contain a variety of chemical constituents like phenols, coumarins, lignans, essential oil, monoterpenes, carotenoids, glycosides, flavonoids, organic acids, lipids, alkaloids and xanthenes3. Recent experience has shown that plant drugs are relatively non-toxic, safe and even free from serious side effects [1, 4].

Liver Diseases: Liver play chief role in regulation of physiological processes. It is involved in several very important functions such as metabolism, secretion and storage. Furthermore, detoxification of a variety of drugs and xenobiotic occurs in liver. The bile secreted by the liver has, among other things, an imperative role in digestion. Liver diseases are among the most serious ailment [4, 6]. They may be classified as acute or chronic hepatitis (inflammatory liver diseases), Liver diseases are mostly caused by toxic chemicals (certain antibiotics, chemotherapeutics, peroxidised oil, aflatoxin, carbon-tetrachloride, chlorinated hydrocarbons, etc.), excess consumption of alcohol, infections and autoimmune/disorder [4,7]. Most of the hepatotoxic chemicals damage liver cells mainly by inducing lipid peroxidation and other oxidative damages in liver. Enhanced lipid per oxidation produced during the liver microsomal metabolism of ethanol may result in hepatitis and cirrhosis [4, 8, 9].

Functions of liver.[10,11].

1. Involve in amino acid synthesis.

2. The liver plays important roles in carbohydrate metabolism.

- Gluconeogenesis (the synthesis of glucose from certain amino acids, lactate or glycerol).
- Glycogenolysis (the breakdown of glycogen into glucose).
- Glycogenesis (the formation of glycogen from glucose) (muscle tissues can also do this)
- The liver is responsible for the mainstay of protein metabolism, synthesis as well as
- Degradation

3. The liver also several roles in lipid metabolism:

- Cholesterol synthesis
- Lipogenesis, the production of triglycerides (fats).

4. The liver produces coagulation factors I (fibrinogen), II (prothrombin), V, VII, IX,

5. The liver produces and excretes bile (a yellowish liquid) required for emulsifying fats.

6. Some of the bile drains directly into the duodenum, and some is stored in the gallbladder.

7. The liver helps in the breakdown of insulin and other hormones

8. It breaks down hemoglobin, creating metabolites that are added to bile as pigmen (bilirubin and biliverdin).

9. The liver produces albumin, the major osmolar component of blood serum

Hepatotoxic Agents [10, 11, 12, 13]

a. Inorganic compounds

Arsenic, Beryllium, Bismuth, Boron, Cadmium, Chromium, Cobalt, Copper, Iron,
Lead, Manganese, Mercury, Gold, Phosphorous, Selenium, Tellurium, Thallium, Zinc, Hydrazine derivative Iodides

Plant toxins: Albitocin, Cycasin, Nutmeg, Tannic acid, Icterogenin, Pyrrolidizines, Saferole, Indospicine.

Mycotoxins: Aflatoxins, Cyclochlorotine, Ethanol, Luteoskyrin, Griseofulvin, Sporidesmin, Tetracycline and Other Antibiotics.

b. Organic compounds

Bacterial toxins: Exotoxins (C.diphtheria, Clostridium botulinus), Endotoxins, Ethionine.

Synthetic: Haloalkanes and Haloolephins, Nitroalkanes, Chloroaromatic compounds, Nitro aromatic compound, Organic Amines, Azo compou Phenol and derivatives,

2. Hepatoprotective plants-

Herbal based therapeutics for liver disorders has been in use in India for a extended time and has been popularized world over by leading pharmaceuticals. Despite the significant popularity of several herbal medicines in general, and for liver diseases in particular, they are still unacceptable treatment modalities for liver diseases. The limiting factors that contribute

I. Lack of standardization of the herbal drugs-
II. Lack of identification of active ingredient(s)/principle(s).
III. Lack of randomized controlled clinical trials (RCTs).
IV. Lack of toxicological evaluation [14]**.**

The use of natural remedies for the treatment of liver diseases has a long history, starting with the Ayurveda treatment, and extending to the Chinese, European and other systems of traditional medicines. A large number of plants and formulations have been claimed to have hepatoprotective activity. Nearly 160 phytoconstituents from 101 plants contain been claimed to possess liver protecting activity [14].

Andrographis paniculata: Andrographolide active constituent of *Andrographis paniculata* (Family of Acanthaceae) antagonized the toxic effects of paracetamol on certain enzymes (SGOT, SGPT and ALP) in serum as well as in isolated hepatic cells as tested by try pan blue exclusion and oxygen

uptake tests, in a significant dose dependent (0.75-12 mg/kg p.o. x 7days) manner 15 .Neoandrographolide increase GSH, glutathione 5-transferase, glutathione peroxidase, SOD and LPO level [14, 15].

***Azadirachta indica*:** Effect of *Azadirachta indica* leaf (Family of Meliaceae) extract on serum enzyme levels (glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acid phosphatase and alkaline phosphatase) elevated by paracetamol in rats was studied with a view to observe any possible hepatoprotective effect of this plant. It is stipulated 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. The antihepatotoxicaction of picroliv seems likely due to an alteration in the biotransformation of the toxic substances resulting in decreased formation of reactive metabolites [14, 16, 17].

Boerhavia diffusa: The hepatoprotective activity of different parts of. *Boerhavia diffusa* Linn. (Nyctaginaceae) The roots of *Boerhavia diffusa* commonly known as 'Punarnava', are used for the treatment of various hepatic disorders.. The hepatoprotective activity of roots of different diameters collected in three seasons, rainy, summer and winter, was examined in thioacetamide intoxicated rats. The results showed that an aqueous extract as the i.v dose of (2 ml/kg) of roots of diameter 1–3 cm, collected in the month of May (Summer), exhibited marked protection of a majority of serum parameters, i.e. GOT, GPT, ACP and ALP, but not GLDH and bilirubin. the aqueous form of drug (2 ml/kg) administration has more hepatoprotective activity than the powder form; this is probably due to the better absorption of the liquid form through the intestinal tract [18,19].

Bauhinia variegate: The alcoholic extract of the bark of the plant *bauhinia variegate* L. was known to produce the hepatoprotective activity. The hepatoprotective activity was investigated in carbon tetrachloride (CCl4) intoxicated Sprague-Dawley rats. *Bauhinia variegata* alcoholic Stem Bark Extract (SBE) at different doses (100 and 200 mg/kg) were administered orally to male Sprague-Dawley rats weighing between 100-120 g. The effect of SBE on the serum marker enzymes, viz., AST, ALT, ALP and GGT and liver protein and lipids were assessed. The extract exhibited significant hepatoprotective activity. Hence, *B. variegata* appears to be a promising hepatoprotective agent [20].

***Curcuma longa*:** *Curcuma longa* is a rhizomatous perennial herb that belongs to the family Zingiberaceae, native to South Asia and is commonly known as turmeric. In Malaysia, commonly known as Kunyit, turmeric plant is a popular ingredient for preparing culinary dishes The hepatoprotective activity of the ethanol extract of the rhizome of *Curcuma longa* was investigated against paracetamol-induced liver damage in rats. At the dose of 600 mg/kg, paracetamol induced liver damage in rats as manifested by statistically significant increase in serum alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) and alkaline phosphatase (ALP). Pretreatment of rats with the ethanolic extract of *Curcuma longa* (100 mg/kg) prior to paracetamol dosing at 600 mg/kg statistically lowered the three serum liver exzyme activities. Moreover, treatment of rats with only the ethanolic extract of *Curcuma longa* (100 mg/kg) had no effects on the liver enzymes. This current results suggest that ethanolic extract of *Curcuma longa* has potent hepatoprotective effect against paracetamol-induced liver damage [21, 22].

Chamomile recutita: *Chamomile recutita* L. Rousch, (family Asteraceae), popularly known as Chamomile is a reputed medicinal and aromatic plant used in both traditional and modern system of medicine *Chamomile recutita* afforded protection from such paracetamol induced liver damage. Possible mechanism that may be responsible for the protection of paracetamol induced liver damage by capitula extract include the following- (a) *Capitula* extract could act as a free radical scavenger intercepting those radicals involved in paracetamol metabolism by microsomal enzymes. (b) A significantly higher content GSH in blood and liver would afford the tissue a better protection against antioxidative stress, thus contributing to the abolishment of paracetamol induced hepatotoxicity [23, 24].

Cocciniagrandis: Alcoholic extract of the fruits of *Cocciniagrandis* Linn (Family of Cucurbitaceae) was evaluated in CCl 4 induced hepatotoxicity in rats and levels of AST, ALT, ALP, total proteins, total and direct bilirubin were evaluated. At a dose level of 250 mg/kg, the alcoholic extract significantly ($p<0.05$) decreased the activities of serum enzymes (AST, ALT and ALP) and bilirubin which were comparable to that of silymarin 20 revealing its hepatoprotective effect [25].

Colchicum autumnale: Colchicine, the major alkaloid in *Colchicum autumnale* (Family of Colchicaceae) protects the liver of experimental animals against several hepatotoxins i.e., D-galactosamine and paracetamol by its ability to

bind microtubule protein. A colchicine derivative, trimethylcolchicinic acid (TMCA) that does not bind tubulin i.e., tested on chronic liver damage induced by CCl 4 and by bile duct ligation (BDL). So, both compounds were equally potent but that TMCA could be administered at larger doses than colchicines without side effects and better hepatoprotective actions [26, 27].

Calotropisprocera: Hydro- ethanolic extract (70 %) of *Calotropisprocera* flowers was prepared and tested for its hepatoprotective effect against paracetamol-induced hepatitis in rats. Alternation in the levels of biochemical markers of hepatic damage like SGPT, SCOT, and ALP, bilirubin, cholesterol, HDL and tissue GSH were tested in both treated and untreated groups. Paracetamol (2 g/kg) has enhanced the SGPT, SGOT, ALP, bilirubin and cholesterol levels and reduced the serum levels of HDL and tissue level of GSH. Treatment with hydro-ethanolic extract of C. procera flowers (200 mg/kg and 400 mg/kg) has brought back the altered levels of biochemical markers to the near normal levels in the dose dependent manner [28].

Ecliptaalba: *Ecliptaalba* (L.) Hassk. (syn.Ecliptaprostratal.) commonly known as false daisy. yerba de tago, and bhringraj, is a plant belonging to the family Asteraceae. The methanolic extract of fresh leaves of the plant Ecliptaalba (Ea) was known to produce hepatoprotective activity. The hepatoprotective potential of the fraction prepared from alcoholic extract was studied in vivo in rats and mice against carbon tetrachloride induced hepatotoxicity. The hepatoprotective activity was determined on the basis of their effects on parameters like hexobarbitone sleep time, zoxazolamine paralysis time, bromosulphaline clearance, serum transaminases and serum bilirubin .it is effective as the oral dose of (10- 80 mg/kg, p.o.) containing coumestanwedelolactone and desmethylwedelolactone as major components with apigenin, luteolin, 4-hydroxybenzoic acid and protocateuic acid as minor constituents exhibited maximum hepatoprotective activity and is the active fraction for hepatoprotective activity of Eclipta alba leave [29,30].

Elytraria acaulis: The *Elytraria acaulis* whole plant hydroalcholic and aqueous extracts were studied for hepatoprotective activity against Swiss albino rats with liver damage induced by carbon tetrachloride (CCl4) [31].

Fumaria indica (Hauskn): *Fumaria indica* (Fumariceae) were studied for their hepatoprotective activity against carbon tetrachloride, paracetamol and rifampicin- induced hepatotoxicities in albino rats. The petroleum ether extract against carbonetrachloride, total aqueous extract against paracetamol and methanolic extract against rifampicin-induced hepatotoxicity showed similar reductions in the elevated levels of some of the serum biochemical parameters in a manner similar that of silymarin indicating its potential as a hepatoprotective agent [32, 33].

Ficus carica: The Methanolic extract of the leaves of *Ficus carica* Linn. (Moraceae) was evaluated for hepatoprotective activity in CCl4 -induced liver damaged rats. The extract at an oral dose of 500 mg/kg exhibited a significant protective effect reflected by lowering the serum levels of AST, ALT, total serum bilirubin, and malon dialdehyde equivalent, an index of lipid peroxidation of the liver [34].

***Glychyrrhiza glabra*:** *Glychyrrhiza glabra* contains triterpene, saponin, known as glycyrrhizin, which has potential hepatoprotective activity. It is belonging to a group of compounds known as sulphate dpolysaccharides. Studied carried out by Japanese researchers have shown glycyrrhizin to be for antiviral and, it has probable for therapeutic use in liver disease [34]. Experimental hepatitis and cirrhosis studies on rats found that it can promote the regeneration of six 6 liver cells and at the same time inhibit fibrosis. Glycyrrhizin can alleviate histological disorder due to inflammation and restore the liver structure and function from the damage due to carbon tetrachloride. Effects of glycyrrhizin have been studied on free radical generation and lipid peroxidation in primary cultured rat hepatocytes. Favourable results have been reported in children suffering from cytomegalovirus after treating with glycyrrhizin [35,36].

Luffaechinata: The different extracts of fruits of *Luffaechinata* Roxb (Cucurbitaceae) were tested for their hepatoprotective activity against CCU induced hepatotoxicity in albino rats. The degree of protection was measured by using biochemical parameters like SGOT, SGPT, alkaline phosphatase and total protein and total albumin. The petroleum ether, methanolic extract showed a significant activity comparable with those of silymarin [37].

Morus nigra: The hepatoprotective activity of methanolic extract of leaves of *Morus nigra* against paracetamol induced. The results showed aqueous methanolic extract of the *Morus nigra* significantly reduced liver enzymes (ALT, AST, ALP) and total bilirubin induced by paracetamol and the results are comparable to silymarin [38].

***Mangifera indica* (Mango):** Mangoes belong to genus Mangifera which consists of about 30 species of tropical fruiting trees in the flowering plant family Anacardiaceae according to Ayurveda. various medicinal properties are attributed to different parts of mango tree Hepatoprotective activities in mango seed kernels studied by Chemo preventive properties of mango pulp extract (MPE) was evaluated in alteration in liver of Swiss albino mice. MPE was found to be effective in combating oxidative stress induced cellular injury of mouse liver by modulating cell-growth [39].

***Morindacitrifolia L*. (noni):** The hepatoprotective effects of Noni juice (TNJ) (Rubiaceae) against CCl(4)-induced chronic liver damage in female Sprague Dawley (SD) rats. Histopathological examination revealed that liver sections from the TNJ + CCl(4) appeared similar to controls, whereas typical hepatic steatosis was observed in the placebo + CCl(4) group. Serum alkaline phosphatase (ALP), aspartate amino transferase (AST), alanine transaminase (ALT), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels were increased in the placebo group compared with the TNJ group. In contrast, high-density lipoprotein (HDL) was increased in the TNJ group anddecreased in the placebo group. Thus, TNJ juice appears to protect the liver from chronic exogenous CCl(4) exposures [40].

Marrubiumvulare L: It exhibited a significant antihepatotoxic activity by decreasing the elevated levels of serum enzymes like SGOT,SGPT,ALP,total protein levels when compared to silymarin against CCL4 induced toxicity in rats. [15,16].

Tylophora Indica: It consists of the dried roots and leaves or rhizomes of *Tylophora Indica* belonging to family Rubeaceae [41].

***Phyllanthusamarus* (Bhuiamala):** Ethanolic extract of *Phyllanthusamarus* (*Euphorbiaceae*), at (0.3g kg (-1) BW 0.2 ml (-1) day (-1) was given to all groups except control groups (gp. I and gp. V), after 30 min of aflatoxin administration. The entire study was carried out for 3 months and animals were sacrificed after an interval of 30 days till the cmpletion of study. *Phyllanthusamarus* extract was found to show hepatoprotective effect by lowering down the content of thiobarbituric acid reactive substances (TBARS) and enhancing the reduced glutathione level and the activities of antioxidant enzymes, glutathione peroxidase (GPx), glutathione-S transferase (GST), superoxide dismutase (SOD) and catalase [15,16].

***Ptrospermumacerifolium* (Kanakchampa):** the hepatoprotective activity of the ethanol extract of the leaf of *Ptrospermumacerifolium* (Sterculiaceae) was investigated in rats. Hepatotoxicity was induced in male Wistar rats by intraperitoneal injection of carbon tetrachloride (0.1 ml/kg/d p.o. for 14 d). Ethanol extract of P. acerifolium leaves were administered to the experimental rats (25 mg/kg/d p.o. for 14d). The Hepatoprotective effect of these extracts was evaluated by liver function biochemical parameters (total bilirubin, serum protein, alanine amino transaminase, alkaline phosphates activites) and histopathological studies of liver. In ethanol extract- treated animals, the toxicity effect of carbon tetrachloride was controlled significantly by restoration of the levels of serum bilirubin and enzymes as compared to the normal and standard drug silymarin-treated groups [15,16].

***Solanumnigrum* (Makoi):** *Solanumnigrum* (Makoi) and Cichoriumintybus (Kasni) The presence of plant extracts of *Solanumnigrum* (solanaceae) 1 kalikhnahaiThe aqueous extract of whole plant of solanumnigrum (SNE) was effective against thioacetamide (TAA)- induced liver fibrosis in mice. It is administered as the dose of (0.2 or 1.0 g/kg). The extract reduced 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 reduced the degree of fibrosis caused by TAA treatment in mice. Probably through the reduction of TGF-β1 secretion [39]. Aqueous extract of SN (ASNE) also evaluated in CCl4 induced chronic hepatotoxicity in rats. Liver histopathology showed that ASNE reduced the incidence of liver lesions including hepatic cells cloudy swelling, lymphocytes infiltration, hepatic necrosis, and fibrous connective tissue proliferation induced by CCl4 in rats. The effect was dependent on the concentration of plant extracts. These studies suggested that the observed hepatoprotective effect of these crude plant extract may be due to their ability to suppress the oxidative degradation of DNA in the tissue debris. Since the herb is commonly known as hepatoprotective agent and have shown these efficacy in protecting against both CCl4 and thioacetamide induced hepatic injury [42].

Swertia Chirata: Due to effect of hepatotoxicant (like ethanol, drugs, chemicals and others) serum aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), and alkaline phosphatase (ALP) activities and bilirubin level are increased, but liver glycogen and serum cholesterol

levels are decreased. Histologically it produced hepatocytic necrosis especially in the centrilobular region. Simultaneous treatments with *Swertia chirata* caused improvement at both biochemical and histopathological parameters. Drug also possesses digestive, hepatic (conditions pertaining to the liver), tonic, astringent and appetizer properties and used in cough, dropsy and skin diseases. Swertia Chirata (Chirayata) Simultaneous treatments with S. Chirata (Gentianceae). (in different doses, viz. 20, 50, and 100 mg/kg body wt daily) and (CCl4) caused improvement at both biochemical and histopathological parameters compared to that of (CCl4) treatment alone but it was most effective when *S. chirata* was administered in a moderate dose (50 mg/kg body wt) [43].

Scutellariarivularis: Baicalein, Baicalin and Wogonin three major components isolated from entire plant of Scutellariarivularis Benth (Family of labiatae); Wogonin (5 mg/kg i.p), exhibit best effect in CCl 4 and D-GalN treated rats. Baicalein and Baicalin at the dose 20 mg/kg i.p in D-GalN and APAP; at dose 10 mg/kg i.p in CCl 4 treated rats exhibit best effect. Protective effects were seen by comparing the serum GOT, GPT and histopathologic examination (hepatic lesion [44].

Silybummarianum: The protective effects of polyphenolic extracts of Sily-bum marianum and Cichoriumintybus on thioacetamide- induced hepatotoxicity in rat was investigated .The extracts were injected to the rats, at a dose of 25 mg kg-1 body weight together with thioacetamide at a dose of 50 mg kg body weight. Significant decrease in the activity of aminotransferase, alkaline phosphatase and bilirubin was observed in the groups treated with extracts and thioacetamide compared with the group that was treated only with thioacetamide. The level of Na+, K+ and liver weight between different groups was not significantly altered. This finding suggested the hepatoprotective effect of *Silybummarianum* and Cichoriumintybus extracts on liver cells due to the presence of flavonoids and their antioxidant effects [15,16].

Taraxacum officinale: Traditionally *Taraxacum officinale* has been used as a remedy for jaundice and other disorders of the liver and gallbladder, and as a remedy for counteracting water retention. Generally, the roots of the plant have the most activity regarding the liver and gallbladder14. Oral administration of extracts from the roots of *Taraxacum officinale* has been shown to act as a cholagogue, increasing the flow of bile. Bitter constituents like taraxecerin and taraxcin are active constituents of the medicinal herb [44].

***Wedeliacalendulacea* L (Bhanra):**
Hepatoprotective activity of the ethanolic-leaf extract of *W.calendulacea* (Asteraceae) (EEWC) was studied by estimating serum enzyme activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), protein and bilirubin. 4 The treatment with EEWC showed a dose-dependent reduction of CCl induced elevated serum levels of enzyme activities with parallel increase in total protein and bilirubin, indicating the extract could preserve the normal functional status of the liver [44].

***Wilkstroemia indica*:** *W. indica* is a Chinese herb and has been evaluated in patients suffering from hepatitis B. A dicoumarin, daphnoretin is the active constituent of the herb. The drug has shown to suppress HbsAG in Hep3B cells. It is said to activator of protein kinase C14 [45].

Z. officinale Daleya: *Z. Officinalis* showed that hepatoprotective activity ($p<0.05$) against inducers, as indicated by an improvement in liver functions test. It concluded that Z.officinale rhizome possess hepatoprotective activity [46].

CONCLUSION

Liver diseases have become one of the major causes of morbidity and mortality in man and animals all over globe and hepatotoxicity due to drugs appears to be the most common contributing factor. About 20,000 deaths found every year due to liver disorders. Many of the modern drugs mainly based on synthetic chemical compounds however have been found to have harmful .side effects in human body. The use of natural remedies for the treatment a large number of medicinal plants have been tested and found to contain active principles with curative properties against a variety of diseases. Liver protective plants contain a variety of chemical constituents like phenols, coumarins, lignans, essential oil etc.

REFERENCE

1 Bhawna S, Kumar SK.Hepatoprotective activity of some indigenous plants,International Journal of PharmTech Research 2009;1330-1334.
2 Bhawna S, Kumar SK.Hepatoprotective activity of some indigenous plants,International Journal of PharmTech Research 2010;568-572.
3 Jain SK et al.Herbal Extract as Hepatoprotective-A Review,Journal of Pharmacognosy and Phytochemistryy 2013; 2 (3): 170-17.
4 Kumar SV.A Review on Hepatoprotective Activity of Medicinal Plants,International journal of advanced research in pharmaceutical and bioscience. 2012; Vol.2 (1):31-38.
5 Kumar et al. A review on hepatoprotective herbal drugs,International journal of research in pharmacy and chemistry 2012; 2(1)
6 Samir S, Hepatotprotective Natural Products 2001; 2(5): 110-111
7 Malhotra S, Hepatotprotective Natural Products 2002; 2 (5):109-115.
8 Ross and Wilson Anatomy and Physiology in Health and illness, Ninth Edition.published by Elsevier Ltd 2010; pp 307-310.
9 Tortora and Grabowski, Principle of Anatomy and Physiology 2003 ;pp 875- 879.
10 Chaterrjee TK.Medicinal Plants with Hepatoprotective Properties. Herbal Options. Books and Applied Allied (P) Ltd, Calcutta, 2000; pp:143
11 Qadrie ZL. Hepatoprotective medicinal herbs and animal models for their screening a review, IJPSR; 2015 612): 5006-5028.
12 Eswar et al.A review on liver disorders and screening models of hepatoprotective agents. Int. J. of Allied Med. Sci. and Clin. Research 2014; 2(2):136-150.
13 Nally M, Peter F. Liver Secrets: with student consult Access. Saint Louis: C.V. Mosby 2006; 618-627.
14 Radha KD, Yogesh KC. Herbal medicines for liver diseases. Digestive Diseases and Sciences 2005; 50(10): 1807–1812.
15 Jannu V et al. A Review on Hepatoprotective Plants,International Journal of Drug Development &Research 2012; 4:25-40.
16 Dahanukar SA et al. Pharmacology of medicinal plants and natural product. Ind J Pharmacol 2000; 32: 81-118.
17 Chattopadhyay RR et al. A Hepatoprotective activity of *Azadirachta indica* leaves on paracetamol induced hepatic damage in rats. Indian J Exp Biol 1992; 30(8):738-4
18 Bhope SG et al. RP-HPLC method for the simultaneous quantitation of boeravinone E and boeravinone B in *Boerhaavia diffusa* extract and its formulation. Nat Prod Res 2012; 27(6): 588-91.
19 Rawat AK et al. Hepatoprotective activity of *Boerhaavia diffusa* L. roots--a popular Indian ethnomedicine. J Ethnopharmacol 1997; 56(1): 61-6.
20 Ajay KG, Neelam M. Hepatoprotective activity of aqueous and ethanolic extract of *boerhaaviaerecta.* incarbontetrachloride intoxicated albino rats. American J PharmacolToxicol 2006;1(1): 17-20.
21 Salama SM et al. Heptatoprotective effect of ethanolic extract of *Curcuma Longa* on Thioacetamide induced liver cirrhosis in rats. BMC Complement Altern Med 2013; 5:13-56.
22 Jannu V et al.A Review on Hepatoprotective Plants,International Journal of Drug Development & Research 2012 ;46-52.
23 Gupta AK, Misra N. Hepatoprotective Activity of Aqueous Ethanolic Extract of *Chamomile capitula* in Paracetamol Intoxicated Albino Rats. Am. J. Pharmacol. Toxicol 2006; 1: 17-28.
24 Dahanukar SA et al. Pharmacology of medicinal plants and natural product. Ind J Pharmacol 2000; 32: 81-118.
25 Vadivu R et al. Evaluation of hepatoprotective activity of the fruits of *Cocciniagrandis* Linn.Int J Health Res 2008; 1(3):163-168.
26 Muriel P et al. Beneficial drugs for liver diseases. J Applied Toxicology 2008; 28:93-103
27 Ramachandra SS et al. Hepatoprotective activity of *Calotropisprocera* flowers against paracetamol-induced hepatic injury in rats Fitoterapia 2007; 78(7-8):451-454.
28 Mei HL et al.Hepatoprotective effects of *Cassia fistula*. Linn extract against CCl4 induced oxidative damage in rats. Chemico-Biological Interactions 2008; 171: 283–293
29 Reddy GVR et al. Preliminary hepatoprotective activity of medicinal plant extracts against carbon tetrachloride induced hepatotoxicity in albino rats, International Journal of Recent Scientific Research 2015 6(7):4946-4951.
30 Rathi Ae.t al. Hepatoprotective potential of *Fumaria indica* Pugsley whole plant extracts, fractions and an isolated alkaloid protopine. Phytomedicine 2008;15(67):470-479.
31 Kumar A. A review on hepatoprotective herbal drugs,International journal of research in pharmacy and chemistry, 2012; 2(1):134-142.
32 Agarwal AK, Mehendale JK. Potentiation of carbon tetrachloride hepatotoxicity and lethality by chlordecone in female rats. Toxicology 1983; 26: 231-42.
33 Trease , Evans, Pharmacognosy. Elsevier Publishers, New Delhi, 2010 pp 414-418.
34 Handa SS. Text Book of Pharmacognosy, VallabhPrakashan, Delhi,2008; pp 202-211.
35 Bahar A et al. Hepatoprotective activity of Luffaechinata fruits. Journal of Ethanopharmaclogoy 2001; 76:87-89
36 Mallhi TH et al. Hepatoprotective Activity Of Aqueous Methanolic Extract of *Morus Nigra* Against Paracetamol Against Paracetamol -Induced Hepatotoxicity In Mice Induced Hepatotoxicity In Mice. Bangladesh J Pharmacol.(2014); 9: 60-66.
37 Kittophom S. Utilization of mango seeds ,international food research journal 2011;(4):1325-1335.
38 Verma A et al. Lead Finding From Whole Plant of *MarrubiumVulgarel*. With Hepatoprotective Potentials Through In Silico Methods. Asian Pacific Journal of Tropical Biomedicine (2012);1308-1311
39 Mujeeb M et al. Hepatoprotective activity of the methanolic extract of *Tylophora indica* (Burm. f.) Merill. leaves. Int J Green Pharms 2009; 3(2):125-127.
40 Kharpate S et al. Hepatoprotective activity of the ethanol extract of the leaf of *Ptrospermumacerifolium*. Indian journal of pharmaceutical sciences 2007; 69(6): 850-52
41 Zeashan H et al.Hepatoprotective activity of *Amaranthusspinosus* in experimental animals.Food ChemToxicol. 2008; 3417–3421.
42 Kokate.CK, Purohit AK, Gokhale.SB, Pharmacognosy, Niraly Prakashan sixth edition 2006 pp 523-525.
43 Ching LC et al. In vivo Hepatoprotective Effect of *Baicalein, Baicalin* and Wogonin from *Scutellariarivular*is .Phytotherapy Research 1996; 10:651-654.
44 Murugaian P et al. Hepatoprotective Activity of *Wedelia calendulacea* L. Against Acute Hepatotoxicity in Rats. Research Journal of Agriculture and Biological Sciences 2008; 4(6):685-87
45 Reddy V et al. A Review on Hepatoprotective Activity of Some Medicinal Plants, International Journal of Innovative Pharmaceutical Research 2014;5(2):395-404.
46 Bardi DA et al. In Vivo Evaluation Of Ethanolic Extract Of *Zingibe Officinale* Rhizomes For Its Protective Effect Against Liver Cirrhosis. Bio Med Research International Volume. (2013); 219-231.