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Plant Based Treatment of Hepatotoxicity

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ABSTRACT: Most of the anti-cancer, anti-tumor and other class of synthetic medicines cause severe adverse effects on the health of human beings especially on the liver. Liver is the organ that metabolizes most of the drugs which are administered orally. While metabolizing other drugs, liver gets affected and synthetic medicines become a cause for liver diseases and hepatotoxicity. According to a report of WHO, about 75 % or three quarters of the world's population use herbs and medicinal plants to cure liver diseases. Plant medicines are with low or zero adverse effects and so can be used by many patients for hepatoprotective effects. Some of the plants which are used as hepatoprotectives are *Andrographic paniculata, Aegle marmelos, Allium sativum, Gymnema sylvestre, Pyrenthrum indicum, Taraxacum officinale, Berberis lyceum, Bryonia alba, Lycopersicon esculentum, Luffa echinata, Nigella sativa, Ocimum sanctum, Terminalia chebula Tinospora cordifolia, and Zingiber officinale* etc. These medicinal plants contain potent phytoconstituents which are of use for the treatment of hepatotoxicity. Therefore in this review, medicinal plants and herbs are collected which are or can be used in liver diseases including hepatotoxicity.
KEYWORD: Liver, Diseases, Hepatotoxicity, Hepatoprotectiv plants etc

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I. INTRODUCTION

Hepatotoxicity

Hepatotoxicity may be defined as the effect of any agent on liver that results in a deviation from normal function, morphology and implies chemical/drug/microbial-driven liver damage.[1]

Hepatotoxicity is one of the main reasons behind withdrawal of a drug from the market. Fifty percent of all acute liver failures and 5% of all hospital admissions are associated with drug-induced hepatotoxicity .[(2)] Liver damage is connectd with alteration of these metabolic functions. Liver damage is associated with cellular necrosis, increase in tissue lipid peroxidation and depletion of reduced glutathione levels. In addition, serum levels of many biochemical

markers like transaminases, alkaline phosphatase, bilirubin, triglycerides and cholesterol are elevated in liver disease [(3)]. Liver diseases pose a serious challenge to international public health.[(4)]

HEPATOTOXICITY CLASSIFICATION

Hepatotoxicity may be classified as the three classes:

(i) the level alanine amino transferase (ALT), that is glutamyl oxalacetic acid transaminase level in the serum increases three‑fold,
(ii) serum alkaline phosphatase (ALP) level increases two‑fold
(iii) serum bilirubin (SBLN) level is also elevated two‑fold (when serum ALT and ALP levels also increases).

Hepatotoxicity is of three major classes:
(a) Hepatocellular injury: When serum ALT or ALP levels are elevated;
(b) Cholestatic injury: When ALP and bilirubin levels in the serum increases;
(c) Mixed injury: When both the ALT and ALP levels in the serum increases.[5]

Liver being closely associated with the gastrointestinal system receives much of the blood from the portal veins, which drains the xenobiotic compounds to the liver. In the liver, the xenobiotic compounds get activated and forms reactive metabolic species (RMS). The RMS through the oxidative stress pathway damage cellular biomolecules, cause protein dysfunctions and damage to the nucleicacids. Mitochondrial dysfunction results due to RMS mediated disruption of ionic gradients and intracellular Ca2+ storage, causing tissue injury.

Hepatocellular inflammation is another outcome of DIHT. Activated natural killer T (NKT) cells and Kupffer cells secret inflammatory mediators such as tumour necrosis factor (TNF)‑α, interferon (IFN)‑γ and interleukin (IL)‑1β also promotes tissue damage.[,6,7,8]

Hepatotoxin is a toxic chemical substance which damages the liver. Toxic liver injury produced by drugs and chemicals may virtually mimic any form of naturally occurring liver disease. Hepatoprotective effect was studied against chemicals and drugs induced hepatotoxicity in rats like alcohol, carbon tetrachloride, galactosamine, paracetamol, isoniazid and rifampicin, antibiotics, peroxidised oil, aflatoxin etc. Severity of hepatotoxicity is greatly increased if the drug is continued after symptoms develop. Among the various inorganic compounds producing hepatotoxicity are arsenic, phosphorus, copper and iron. The organic agents include certain naturally occuring plant toxins such as pyrrolizidine alkaloids, myotoxins and bacterial toxins.[9]

Traditional plants play a important role in the human health care ailmetns. 80% of world populations depend on traditional medicines .Traditional medicines principally based on plant materials [10]. The traditional medicine including folk and tribal follows as well as AYUSH (Ayurveda, Siddha, Amchi, Unani) . The traditional medicine refers to a broad range of ancient natural health care. AYUSH medical practices originated from time immemorial and developed gradually, significantly, by relying or derived from practical experiences devoid of important references to modern scientific principles. These practices incorporated ancient beliefs and were passed on from one generation to another by oral tradition and/or guarded literature. While herbal medicines are effective in the treatment of various ailments very often these drugs are unscientifically exploited and/or improperly used. Therefore, these plant drugs deserve detailed studies in the light of modern science.

Plants are used in India mostly (rural , tribal villages) about 7,500 plants in local health traditions. About 1,200 plants are use in classical system of medicine such as as Ayurveda, Siddha, Amchi, Unani and Tibetan[11].

A completed exploration and certification of plants used in local health traditions and pharmacological evaluation of these plants .Plants and their taxonomical links can lead to the development of invaluable plant drugs for many dreaded diseases. Random screening of plants has not proved economically effective[12,13].

Liver diseases and medicinal plants:

Liver is the main organ, play a essential role in regulation of physiological processes. Liver engaged in numerous fundamental functions such as metabolism, secretion and storage. Also, liver detoxified of a selection of drugs and xenobiotics occurs in liver. An important role of liver in digestions. The bile secreted by the liver has, among other things.[14] Liver injury caused by different infections, certain drugs, environmental and social factors such as alcoholism[5] resulting in severe pathological conditions such as hepatitis, liver cirrhosis, hepatosis (non inflammatory diseases)[15] etc.

Liver diseases are surrounded by the majority serious disease. Drugs and chemicals can cause a broad spectrum of liver injury. These consist of:

Mild elevations in blood levels of liver enzymes without symptoms or signs of liver disease

Hepatitis (inflammation of liver cells), **Necrosis** (death of liver cells) that often is caused by more severe hepatitis, **Cholestasis** (decreased secretion and/or flow of bile)

Steatosis (accumulation of fat in the liver), **Cirrhosis** (advanced scarring of the liver) as a result of chronic hepatitis, cholestasis, or fatty liver, **Mixed disease**, for example both hepatitis and necrosis of liver cells, hepatitis and fat accumulation, or cholestasis and hepatitis., **Fulminant hepatitis** with severe, life threatening liver failure, **Blood clots** in the veins of the liver

Liver diseases are mainly caused by toxic chemicals certain antibiotics like Augumentin , cilndamycin, erythromycin, chemotherapeutics likes asparaginase, nitrosureas, vinblastine, peroxidised oil, aflatoxin, carbon-tetrachloride, chlorinated hydrocarbons, etc.), excess consumption of alcohol, infections and autoimmune/disorder.[16]

The hepatotoxic chemicals damage liver cells primarily by inducing lipid peroxidation and other oxidative damages in liver. During the liver microsomal metabolism of ethanol, productions of lipid peroxidation increased, caused hepatitis and cirrhosis.[17] It has been approximated that about 90% of the acute hepatitis is due to viruses. The major viral agents involved are Hepatitis B, A, C, D, E and G. Chronic liver diseases and cirrhosis of liver result occure with hepatitis B infection. Hepatitis B virus has also been produced Primary liver cancer.

It has been estimated that approximately 14- 16 million people are infected with this virus in South East Asia region and about 6% of the total population in the region are carriers of this virus. A vaccine has become available for immunization against Hepatitis B virus. Hepatitis C and Hepatitis E infections are also common in countries of South East Asia region.

Liver diseases which are still a global health problem may be classified as acute or chronic hepatitis, hepatosis and cirrhosis, Unfortunately, treatments of choice for liver diseases are controversial because conventional or synthetic drugs for the treatment of these diseases are insufficient and sometimes cause serious side effects. The WHO find out the data around 2.4 million deaths yearly are linked to some liver disease, and that around 800 thousand of these deaths are attributable to cirrhosis.

II. METHODS

Some important hepatoprotective medicinal plants mentioned in Ayurveda:

FAMILY	PLANTS NAME	PARTS USED
Acanthaceae	*Andrographic paniculata* (Burm.f.) Wall. ex Nees *Asteracantha longifolia* Nees.	Whole plant Leaf, root and seed
Asclepiadaceae	*Hemidesmus indicus* R.Br. *Gymnema sylvestre* (Retz.) R.Br.ex Schult	Root Leaf
Asteracceae	*Taraxacum officinale* F.H. Wigg *Pyrenthrum indicum* DC. *Cichorium intybus* L.	Root Flower Whole plant
Berberidaceae	*Berberis lycium* Royle	Leaf
Cucurbitaceae	*Bryonia alba* Wild Hops Root *Luffa echinata* Roxb. Fruit and seed	Root Fruit and seeds
Euphorbiaceae	*Euphorbia neriifolia* L.	Fruit
Fumariaceae.	*Fumaria officinalis* L.	Whole plant
Guttiferae	*Garcinia indica* (Linn.) Robs.	Fruit
Gentianaceae	*Swertia chirata* (Wall.) C. B. Clarke	Whole plant
Labiatae	*Mentha longifolia* (L.) Huds	Leaf
Nymphaceae	*Nelumbo nucifera* Gaertn.	Flower
Menispermaceae	*Tinospora cordifolia* (Willd.) Hook. f.	Stem
Solanceae	*Lycopersicon esculentum* L.	Fruit
Zingiberaceae	*Zingiber officinale* Roxb.	Rhizome

Andrographic Peniculata

Hygrophila spinosa T. Ander.

Nelumbo nucifera Gaertn.

Gymnema Sylvestris

Pyrenthrum Indicum

Berberis lycium Royle

Zingiber officinale Roxb.

Apium graveolens L.

Lycopersicon esculentum L.

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Rumex crispus L.

Tinospora cordifolia (Willd.)

Mentha longifolia (L.) Hud

List of hepatoprotctive plants:

SL. No.	Botanical name	Botanical plant (Family)	Parts used	Extract	Hepatotoxic agent	*In vivo* models	Remarks about liver marker enzymes	References
1	*Abutilon bidentatum*	*(Malvaceae)*	Leaves, Flowers	Aqueous methanol	PCT and CCl4	Rabbit	↓ SGPT, SGOT, ALKP and DB	19
2	*Aegle marmelos*	*(Rutaceae)*	Leaves	Ethanol	CCl4	Mice	↓ SGPT, SGOT, ALP and DB	20
3	*Aerva lanata*	*(Amaranthaceae)*	Leaves	Hydro-alcoholic	PCT	Rat	↓ levels of AST, ALP, DB and serum TB	21
4	*Allium sativum*	*(Liliaceae)*	Fruit	No extract	INH	Rat	↓ AST, ALP, SGPT, SGOT and DB	22
5	*Alcea rosea*	*(Malvaceae)*	Aerial parts	Aqueous methanol	PCT	Mice	↓ levels of AST, ALP, DB and serum TB	23
6	*Aloe barbadensis*	*(Liliaceae)*	Aerial parts	Chloroform, ether and petroleum	CCl4	Mice	↓ AST, ALP and ALT levels. Restored depleted liver thiols	24
7	*Aloe vera*	*(Liliaceae)*	Leaves	Aqueous	gamma-hexachlorocyclohexane (Lindane)	Mice	↓ AST, ALP and ALT levels. Restored depleted liver thiols	25
8	*Amaranthus caudatus*	*(Amaranthaceae)*	Whole plant	Methanolic extract	PCT	Rat	↓ ALT, AST, DB, TB and MDA level. ↑ ALB, GSH, TT, TP and CT Levels	26
9	*Amaranthus spinosus*	*(Amaranthaceae)*	Whole plant	Ethanol	CCl4	Rat	↓ ALT, AST, DB, TB and MDA level. ↑ ALB, GSH, TT, TP and CT Levels	27
10	*Annona squamosa*	*(Annonaceae)*	Leaves	Aqueous ethanol	INH	Rat	↓ TB, ALP, AST, ALT and γ-GT and ↑ TP level	28
11	*Arachniodes exilis*	*(Dryopteridaceae)*	Rhizome	Ethanol	CCl4	Mice	↓ AST, ALT, ALP and CHL. ↑ antioxidant enzyme activities of SOD, CAT, MDA and GSH	29
12	*Asparagus racemosus*	*(Liliaceae)*	Whole plant	Crude aqueous	PCT	Rat	↑ LPO, ↓ GSH and SOD	30
13	*Baliospermum montanum*	*(Euphorbiaceae)*	Leaves	Alcohol, Chloroform	Thioace-tamide	Mice	↓ in SGOT , SGPT and CHL level	31
14	*Berberis lyceum*	*(Berberidaceae)*	Bark	Alcohol	CCl4	Rat	↓ TB, ALP, AST, and ALT levels	32

15	*Bixa orellana*	*(Bixaceae)*	Seed	Methanol	CCl4	Rat	↓ in SGOT , SGPT and cholesterol level	33
16	*Boerhaavia diffusa*	*(Nyctaginaceae)*	Roots	Aqueous	Thioace-tamide	Rat	↓ TB, ALP, AST, and ALT and ↑ TP	34
17	*Bombax ceiba*	*(Bixaceae)*	Flowers	Methanol	INH, RMP	Rat	↓ TB, ALP, AST, and ALT and ↑TP	35
18	*Bupleurum kaoi*	*(Umbelliferae)*	Roots	Ethanol	Dimethyl nitrosamine	Rat	↓ SGOT , SGPT, ALP, AST and ALT	36

19	*Butea monosperma*	*(Fabaceae)*	Flowers	Aqueous	PCT	Rabbit	↓ ALP, AST and ALT	37	Maaz et al., 2010
20	*Cajanus cajan*	*(Fabaceae)*	Whole plant	Methanol	CCl4	Rat	↓ SGOT , SGPT and CHL level	38	Sing et al., 2011
21	*Calotropis procera*	*(Apocynaceae)*	Flower	Aqueous alcohol	PCT	Rat	↓ SGPT, SGOT, ALP, bilirubin and LDLP, ↑ serum levels of HDL and tissue level of GSH.	39	Setty et al., 2007
22	*Carica papaya*	*(Caricaceae)*	Fruit	Aqueous ethanol	CCl4	Rat	↓ SGOT , SGPT, ALP, AST, ALT and LDH Levels	40	Sadeque and Begum, 2010
23	*Carissa opaca*	*(Apocynaceae)*	Leaves	Methanol	CCl4	Rat	↓ lipid peroxidation (TBARS), AST, ALT, ALP, LDH and γGT Levels	41	Sahreen et al., 2011
24	*Carissa spinarum*	*(Apocynaceae)*	Roots	Ethanol	PCT and CCl4	Rat	↓ SGOT , SGPT, ALP, AST, ALT and LDH Levels	42	Hegde and Joshi, 2010
25	*Cassia fistula*	*(Leguminaceae)*	Leaves	Ethanol	N-heptane	Rat	↓ ALP, AST, ALT, LDH and γ-GT	43	Bhakta et al., 2001
26	*Cassia occidentalis*	*(Caesalpiniaceae)*	Leaves	Aqueous ethanol	PCT	Rat	↓ SGOT , SGPT, ALP, AST, ALT and LDH Levels	44	Rani et al., 2010
27	*Casuarina equisetifolia*	*(Casuarinaceae)*	Leaves and Bark	Methanol	CCl4	Rat	↓ SGOT , SGPT and cholesterol level	45	Ahsan et al., 2009
28	*Cestrum nocturnum*	*(Solanaceae)*	Leaves	Aqueous ethanol	PCT	Mice	↓ SGOT , SGPT, ALP, AST, ALT and LDH Levels	46	Qadir et al., 2014
29	*Chamomile recutita*	*(Asteraceae)*	Flower	Methanol	CCl4	Rat	↑ Conc. of glutathione in Liver & blood and Na+K+ATPase activity. ↓ ALT, AST, ALP, TB and liver glycogen levels	47	Gupta et al., 2006
30	*Chenopodium murale*	*(Chenopodiaceae)*	Whole plant	Aqueous methanol	PCT	Mice	↓ ALP, AST, ALT and TB levels	48	Saleem et al., 2014

31	*Cinnamomum tamala*	*(Lauraceae)*	Leaves	Methanol	PCT	Mice	↓ SGOT, SGPT, ALP, lipid profile, TB and ↑ TP	49	Selvam et al., 2010
32	*Clerodendron inerme*	*(Verbenaceae)*	Leaves	Ethanol	PCT	Rat	↓ SGOT, SGPT, SALP, TB and ↑ TP levels	50	Haque et al., 2011
33	*Coccinia grandis*	*(Curcubitaceae)*	Leaves	Aqueous, Ethanol	CCl4	Rat	↓ SGOT, SGPT, ALP, TB and CHL levels	51	Sunilson et al., 2009
34	*Cocculus hirsutus*	*(Menispermaceae)*	Aerial parts	Methanol	Bile duct ligation	Rat	↓ ALT, AST, LDLC, HDL TC and STG. ↑ antioxidant enzyme activities of SOD, CAT, GSH-Px and GST	52	Thakare et al., 2009
35	*Cochlospermum planchoni*	*(Coclospermaceae)*	Rhizome	Aqueous	CCl4	Rat	↓ ALP, AST and TB Levels	53	Nafiu et al., 2011
36	*Convolvulus arvensis*	*(Convolvulaceae)*	Whole plant	Ethanol	PCT	Mice	↓ ALP, AST, ALP and TB levels	54	Ali et al., 2013

37	*Cordia macleodii*	*(Boraginaceae)*	Leaves	Ethanol	CCl4	Rat	↓ SGPT, SGOT, ALP and TB levels	55
38	*Cuscuta chinensis*	*(Convolvulaceae)*	Seeds	Aqueous ethanol	PCT	Rat	↑ antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH	56
39	*Cyathea gigantea*	*(Cyatheaceae)*	Leaves	Methanol	PCT	Rat	↓ SGPT, SGOT, ALP,TB, TP and reverse the hepatic damage	57
40	*Decalepis hamiltonii*	*(Asclepiadaceae)*	Roots	Aqueous	Ethanol	Rat	↓ ALT, AST, LDLC, HDL TC and STG. ↑ SOD, CAT, GSH-Px, GST, and GSH	58
41	*Dodonaea viscose*	*(Sapindaceae)*	Leaves	Methanol	Alloxan	Rabbit	↓ ALT, AST, LDLC, HDL TC and STG	59
42	*Eclipta alba*	*(Asteraceae)*	Whole plant	Ethanol	PCT	Mice	↓ ALT level, fatty degeneration and centrizonal liver Necrosis	60
43	*Emblica officinalis*	*(Phyllanthaceae)*	Leaves	Ethanol	CCl4	Rat	↓ ALT, AST, LDLC, HDL TC and STG	61
44	*Equisetum arvense*	*(Equisetaceae)*	Aerial parts	Methanol	Tacrine	Hep G2 cells	↓ AST, ALT, TP, TB and ALP levels	62
45	*Eucalyptus maculata*	*(Myrtaceae)*	Leaves	Chloroform	PCT	Rats and Mice	↓ AST, ALT and ALP	63
46	*Euphorbia fusiformis*	*(Euphorbiaceae)*	Tubers	Ethanol	RMP	Rat	↓ AST, ALT, ALP, SGPT and SGOT	64
47	*Feronia elephantum*	*(Rutaceae)*	Fruit	Aqueous	CCl4	Rat	↓ ALT, AST, billirubin level and ↑ TP levels	65
48	*Ficus cordata*	*(Moraceae)*	Roots	Methanol/ ethylacetate	CCl4	Rat	Prevent liver cell death and LDH leakage	66
49	*Foeniculum vulgare*	*(Apiaceae)*	Leaves and fruit	Ethanol	CCl4	Rat	↓ AST, ALT, ALP, SGPT and SGOT	67
50	*Galium aparine*	*(Rubiaceae)*	whole plant	Alcohol	CCl4	Rat	↓ALP, AST, and ALT Levels	68

51	*Glycosmis pentaphylla*	*(Rutaceae)*	Leaves and bark	Methanol	PCT	Mice	↓ in SGOT , SGPT and cholesterol level	69
52	*Glycyrrhiza glabra*	*(Fabaceae)*	Roots	Aqueous	CCl4	Rabbit	↑ antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH	70
53	*Gundelia tourenfortii*	*(Asteraceae)*	Stalk	Hydro alcoholic	CCl4	Rat	↓ALP, AST, TB and ALT Levels	71

54	*Halenia elliptica*	*(Gentianaceae)*	Whole plant	Methanol	CCl4	Rat	↓ SGOT, SGPT, ALP, AST and TB levels	72
55	*Haloxylon salicornicum*	*(Chenopodiaceae)*	Aerial parts	Ethanol	CCl4	Rabbit	↓ SGOT, SGPT, ALP and TB levels	73
56	*Hemidesmus indicus*	*Apocynaceae*	Roots	Methanol	INH and RMP	Rat	↓ ALP, AST, TB and ALT	73
57	*Hygrophila auriculata*	*(Acanthaceae)*	Roots	Aqueous	CCl4	Rat	↓ AST , ALT, ALP, TB and CHL levels	73
58	*Hypericum japonicum*	*(Clusiaceae)*	Whole plants	Aqueous	CCl4	Mice	↓ SGPT, SGOT, AST , ALT and ALP levels	74
59	*Hyptis suaveolens*	*(Lamiaceae)*	Leaves	Aqueous	PCT	Rabbit	↓ TP and TB levels	75
60	*Ipomoea staphylina*	*(Convolvulaceae)*	Levaes	Hydro- alcohol	CCl4	Rat	↓ALP, AST, ALT, SGPT, SGOT and CHL levels	76
61	*Kohautia grandiflora*	*(Rubiaceae)*	Leaves	Aqueous	PCT	Rat	↓ AST , ALT, ALP, TB and TP	77
62	*Laggera pterodonta*	*(Asteraceae)*	Whole plant	Ethyl alcohol	CCl4	Rat	↓ AST , ALT, ALP, TB and TP	78
63	*Launaea procumbens*	*(Asteraceae)*	Whole plant	Methanol	CCl4	Rat	↓ ALT, AST, ALP, LDH, LDL, HDL, TC and Triglycerides levels	79
64	*Lepidium sativum*	*(Brassicaceae)*	Whole plant	Methanol	CCl4	Rat	↓ AST , ALT, ALP, TB and TP	80
65	*Luffa echinata*	*(Cucurbitaceae)*	Fruit	Petroleum, acetone and methanol	CCl4	Rat	↓ SGOT, SGPT, ALP and AST levels	81
66	*Momordica dioica*	*(Cucurbitaceae)*	Leaves	Aqueous methanol	CCl4	Rat	↓ ALP, AST, TP and ALT	82
67	*Mimosa Pudica*	*(Mimosaceae)*	Leaves	Methanol	CCl4	Rat	↓ AST , ALT, ALP, TB and TP. ↓ SGOT, SGPT	83
68	*Moringa oleifera*	*(Moringaceae)*	Roots, flowers	Methanol	INH, RMP, PZA	Rat	↑ Antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH. ↓ AST , ALT,	84

							ALP, TB and TP. ↓ SGOT, SGPT	
69	*Nigella sativa*	*(Ranunculaceae)*	Seeds	Alcohol	Galactosa-mine/ lipo-polysaccharide	Rat	↓ALP, AST, TB, TP and ALT	85
70	*Ocimum sanctum*	*(Lamiaceae)*	Leaves	Alcohol	PCT	Rat	↓ SGPT, SGOT, ALT, AST and ALP	86
71	*Phoenix dactylifera*	*(Arecaceae)*	Fruits	Methanol	Thioaceta-mide	Rat	Ameliorated the increased level of MDA and decline of GSH and amelioration of ALT, ALP and AST	87
72	*Parkinsonia aculeata*	*(Fabaceae)*	Leaves	Ethanol	PCT	Rat	↓ SGOT, SGPT, LDH, ALP, TB and ↑ TP levels	88
73	*Phyllanthus polyphyllus*	*(Euphorbiaceae)*	Leaves	Methanol	PCT	Mice	↓ ALP, AST, ALT, SPGT and SGOT levels. ↑ Antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH.	87
74	*Physalis minima*	*(Solanaceae)*	Whole plant	Methanol	CCl4	Rat	↓ SGPT, SGOT, LPO, TP, ALT, AST and ALP	89
75	*Piper chaba*	*(Piperaceae*	Fruit	Aqueous acetone	Galactosa-mine/lipo-polysaccha-ride	Mice	↓ALP, AST, ALT, SGPT and SGOT levels	90
76	*Picrorhiza kurroa*	*(Scrophulariaceae*	Roots rhizomes	Ethanol	CCl4	Rat	↓ALP, AST, ALT, SGPT, SGOT and CHL levels	91
77	*Phyllanthus emblica*	*(Euphorbiaceae)*	Fruits	Aqueous	PCT	Rat	Significant ↑ TBC and less necrosis	92
78	*Pistacia integerrima*	*(Anacardiaceae)*	Bark	Ethyl acetate	PCT	Rat	↓ ALP, AST, and ALT levels	93
79	*Plumbago zeylanica*	*(Plumbaginacea)*	Aerial parts	Methanol	PCT	Rat	↓ serum TB, SGPT, SGOT and ALP levels	94
80	*Physalis minima*	*(Solanaceae)*	Whole plant	Methanol	CCl4	Rat	↓ SGPT, SGOT, LPO, TP, ALT, AST and ALP	95
81	*Phyllanthus niruri*	*(Euphorbiaceae)*	Leaves, fruits	Aqueous methanol	PCT	Mice	↑ Antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH.	96

82	*Rubia cordifolia*	*(Rubiaceae)*	Roots	Methanol	Thioactami de	Rat	↓ ALP, AST, ALT , SPGT and SGOT levels	97
83	*Rumex dentatus*	*(Polygonaceae)*	Whole plant	Aqueous-methanol	PCT	Mice	↓ ALP, AST, TB and ALT levels	98
84	*Rheum emodi*	*(Polygonaceae)*	Roots	Petroleum benzene, chloroform	CCl4	Rat	↓ serum TB, TP, SGPT, SGOT, AST and ALP levels	99
85	*Rosa damascene*	*(Rosaceae)*		Aqueous methanol	CCl4	Rat	↓ SGPT, SGOT, LPO, TP, ALT, AST and ALP levels.	Achuthan et al., 2003
86	*Solanum nigram (Solanaceae*	*Solanaceae*	Fruit	Ethanol	CCl4	Rat	↓ AST, ALT, ALP, TP and TB levels	Raju et al., 2003
87	*Terminalia chebula*	*Combetraceae*	Fruit	Ethanol	RIF, INH, PZA	Rat	↓ AST, ALT, ALP, TP and TB levels	Tasduq et al., 2006
88	*Tylophora indica*	*Asclepiadaceae*	Leaf powder	Aqueous alcohol	Ethanol	Rat	↓ AST, ALT, ALP, TP and TB levels	Gujrati et al., 2007
89	*Vitis vinifera*	*Vitaceae*	Roots	Ethanol	CCl4	Rat	↓ SGOT, SGPT, TB, AST, ALP levels. ↑ CAT and GSH levels	Sharma et al., 2012
90	*Zanthoxylum armatum*	*Rutaceae*	Bark	Ethanol	CCl4	Rat	↓ SGOT, SGPT, TB, AST, ALP, ↑ CAT, GSH levels	Verma et al., 2010

III. CONCLUSION

Liver diseases which are still a global health problem may be classified as acute or chronic hepatitis, hepatosis and cirrhosis. Liver diseases are mainly caused by toxic chemicals such as certain antibiotics like cilndamycin, erythromycin, chemotherapeutics likes asparaginase, nitrosureas, vinblastine, peroxidised oil, aflatoxin, carbon-tetrachloride, chlorinated hydrocarbons, etc. Excess consumption of alcohol, also affects liver. Unfortunately, treatments of choice for liver diseases are controversial because conventional or synthetic drugs for the treatment of these diseases are insufficient and sometimes cause serious side effects. The WHO find out the data around 2.4 million deaths yearly are linked to some liver disease, and that around 800 thousand of these deaths are attributable to cirrhosis. Plant based crude drugs and herbal medicines are need of the hour. Medicinal plants can be used for the treatment of hepatotoxicity because they cause minor or zero said effects and also they have potent phytoconstituents like anti oxidant flavonoides, alkaloids, glycosides, which are beneficial to cure liver insufficiency.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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