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A review on hepatoprotective activity of Indian traditional plant

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Abstract
The liver is an essential organ that aids in the metabolism and elimination of xenobiotics from the body. Liver damage or liver dysfunction, is a serious health issue that concerns not only doctors, but also the pharmaceutical companies and drug regulatory bodies. The effects of numerous hazardous substances (particular antibiotics, chemotherapeutics, carbon tetrachloride (CCl4), thioacetamide (TAA), and microorganisms on liver cells have been extensively researched. Synthetic drugs used to treat liver abnormalities in this condition can also harm the liver in other ways. Synthetic drugs used to treat liver abnormalities in this condition can also harm the liver in other ways. As a result, herbal medications are becoming increasingly popular, and their use is becoming more prevalent. The use of medicinal plants in the treatment of liver illness has a long history. On the market, there are a variety of herbal preparations. The goal of this review is to gather information on prospective phytochemicals from medicinal plants that have been investigated in modern scientific hepatotoxicity models.

Keywords: hepatoprotective, plant, liver

Introduction

The liver is one of the human body's most important organs, as it is the primary place for regulating metabolism and excretion. The liver is the body's second largest organ, weighing roughly 1.5 kg in adults, or 2% of total body weight [1]. It is responsible for the generation and excretion of bile, as well as the excretion of bilirubin, cholesterol, hormones, medications, proteins, and the metabolism of fats and carbohydrates. The liver's digestive fluid plays an important function in digesting, among other things [2]. The liver's physiological activity produces highly reactive free radicals with different molecular species in which an atomic constituent's unpaired valence electron does not contribute to binding inside free radical molecules. They are highly reactive due to the presence of free electrons from reactive oxygen species (ROS) [3]. Aging, energy production, the immune system, metabolism, toxins, and medicines are all primary sources of free radical generation in the body. Through covalent connections, free radicals attach to membrane lipids and cause lipid peroxidation [4]. Many chemicals, such as some chemotherapy medications, carbon tetrachloride, thioacetamide, and others, as well as persistent alcohol intake and microorganisms, cause damage to liver cells. Increased peroxidation of super molecules during alcohol metabolism may contribute to the development of liver disease [5]. Several earlier studies have found that liver damage increases the production of extracellular matrix proteins by liver stellate cells (ECM). An imbalance in the synthesis and usage of ECM results in an excessive accumulation of ECM, which leads to liver fibrosis [6]. Cirrhosis is an advanced stage of liver fibrosis with normal vascular structure and disrupted parenchyma, which can be caused by liver fibrosis. Several investigations have demonstrated, however, that liver fibrosis and even cirrhosis are pathologically reversible and can be prevented early on. [7].

For decades, natural products have played an important role in healthcare. Plants have been a source of the chemical, functioning as full-fledged medications or important elements in formulations comprising synthetic drugs, and are often distinct sources of natural medicines [8]. The plant species chosen is a critical aspect in the research's possible success. Certain clues are revealed through random selection, and focused collection based on chemotaxonomic correlations and ethnomedical information gained from traditional medicine are more likely to yield pharmacologically active substances [9].

Despite advancements in modern medicine, herbal remedies continue to be in high demand. Before they may be validated for disease treatment, effective and potent herbal medicines must be evaluated using standard scientific methodologies [10].

Herbal medications are more extensively utilised as hepatoprotective treatments than allopathic medicines because they are less expensive, have a higher cultural acceptability, are more compatible with the human body, and produce minimal side effects. These natural medications have demonstrated the ability to preserve normal and useful liver stats while causing fewer adverse effects [11].

Causes of Hepatotoxicity

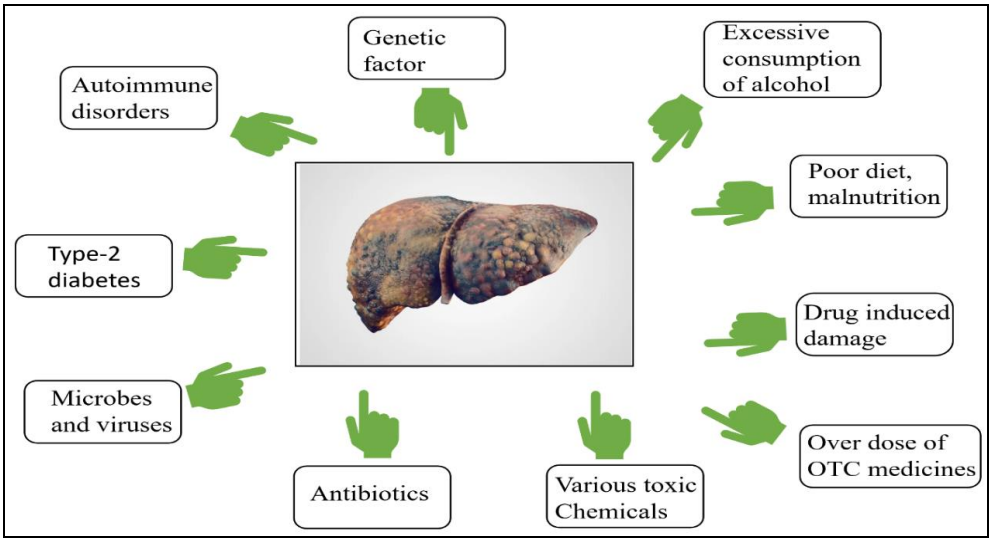

Fig 1: Common Causes of Hepatotoxicity

Mechanism of Hepatotoxicity

The bioactivation of medicines into chemically reactive metabolites, which can interact with cellular macromolecules like proteins, lipids, and nucleic acids, causing protein malfunction, lipid peroxidation, DNA damage, and stress oxidative stress, causes liver damage. [12].

Furthermore, these reactive metabolites can cause ionic grad ients and intracellular calcium
reserves to be disrupted, resulting in mitochondrial malfunct ion and energy production loss.

Its malfunction causes an excess of oxidants, which damage liver cells [13]. Oxidative stress is also caused by the activation with cytochrome P-450 system enzymes, such as CYP2E1. Bile acid builds up inside the liver due to damage to hepatocytes and bile duct cells. This causes the liver to be damaged even more. This change in cell function can result in cell death [14].

In addition to triggering innate and adaptive immune responses, liver cell malfunction and death can also induce immunological responses. Hepatocyte stress and damage trigger the release of signals that activate other cells, particularly those of the innate immune system, such as Kupffer cells (KC), or natural killer cells (NK) [15]. These cells reduced the progress of liver injury by secreting chemokines and generating pro-inflammatory mediators that attracted more inflammatory cells to the liver. Several inflammatory cytokines released during liver injury, such as tumour necrosis factor (TNF)-α interferon (IFN)-γ, and interleukin (IL) -1β, have been implicated in the promotion of tissue destruction. [16].

Innate immune cells, on the other hand, are the main source of IL-10, IL-6, and certain prostaglandins, all of which have been demonstrated to have hepatoprotective properties. As a result, an individual's sensitivity and response to liver damage is determined by the delicate balance of inflammatory and hepatoprotective mediators released after activation of the innate immune system [17].

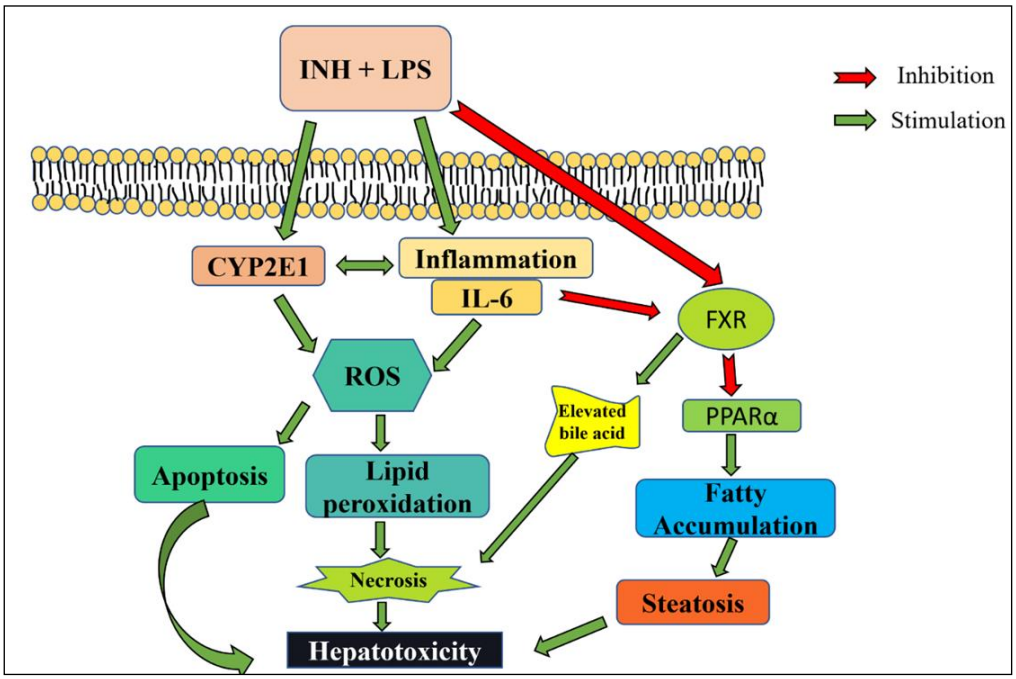

Fig 1: Mechanism of Hepatotoxicity

Liver Function Test

- The following enzymes are included in standard liver fu nction tests (LFTs).
- Alanine Transaminase (ALT)
- Aspartate Transaminase (AST)
- Alkaline Phosphatase (ALP)
- Serum Glutamic-Pyruvic Transaminase (SGPT)
- Serum Glutamic-Oxaloacetic Transaminase (SGOT)
- Gamma Glutamyl Transferase (GGT), Together with
- Bilirubin
- Albumin
- Total Protein and
- Globulin.

Table 1: Hepato protective Plants

Plant	Common name	Family	Parts used	Hepatotoxicant	Extract used	Bioactive constituents	Evaluate histological parameters
Thalictrum Foliolosum [18]	Leafy Meadow-Rue	Ranunculaceae	Root	Paracetamol	Ethanolic	Alkaloids (berberine, jatrorrhizine, palmatine, thalrugosidine, thalrugosaminine, thalisopine thaligosine, thalirugidine, trhalirugine, 8-oxyberberine, berlambine	ALT, ASP, AST
Ipomoea staphylina Linn [19]	Clustered Morning Glory	Convolvulaceae	Leaves	CCl4	aqueous extract	Ergotamine, Ergometrine, Ergine, Ergoline, Ergonovine	SGOT, SGPT, ALP and bilirubin.
Cucumis ficifolius [20]	Cucumis	Cucurbitaceae	Root	CCl4	methanol crude extract		
Solanum nigrum [21]	Black nightshade	Solanaceae	Leaves and berries	D-Galactosamine	Hydroalcoholic	Solanine, Sapogenin, Solanidine, Solamargine, Diosgenin	ALT, AST, ALP,
Phyllanthus niruri [22]	Stonebreaker	Phyllanthaceae	aerial parts	CCl4	aqueous extract	Geraniin, Corilagin, Securinine, Lupeol, Astragalin,	AST, ALT, GSH, and SOD levels
Dypsis lutescens [23]	Yellow palm	Arecaceae	leaves	D-galactosamine	ethanolic extract	Luteolin, Prechafuroside, orientin, iso orientation	GOT, GPT, ALP, MDA
Moringa oleifera [24]	Drumstick	Moringaceae	Bark	Paracetamol	Ethanolic	Quercetin, apigenin, kaempferol, and isorhamnetin	GPT/ALT, GOT/AST, ALP, Total bilirubin, Total protein
Prunella vulgaris [25]	Selfheal	Lamiaceae	Floral spikes	Paracetamol	Hydro alcoholic	ursolic acid, β-amyrin, quercetin, α-spinasterol, stigmasterol, β-sitosterol, daucosterol.	SGPT, SGOT, ALP, Total protein, Direct bilirubin
Anbara [26]	Dates	Arecaceae	Fruits	CCl_4	Aqueous	Palmitic acid, Syringic acid, Procyanidin, Fructose, β-carotene, p-coumaric acid, ferulic acid, sinapic acids,	AST, ALP, ALT, RBC, WBC, MCV, Hb,
Aerva sanguinolenta [27]	Mountain knotgrass	Amaranthaceae	Whole plant	Acetaminophen	Ethanolic	Ferulic acid, Syringic acid, Narcissin, Feruloyltyramine, sitosteryl palmitate, α-amyrin, botulin, β-Sitosterol	GOT, GPT, ALP, LDH
Tectona grandis [28]	Teak	Lamiaceae	Bark	CCl_4	Ethanolic	Phthalic acid, n-hexadecanoic acid, 9-Octadecenoic acid	SGPT, SGOT, ALP, Total bilirubin
Hippophae rhamnoides [29]	Sea buckthorn	Elaeagnaceae	Leaf	Lead acetate	Aqueous	Vitamin C, Carotenoids, L-ascorbic,Quercetin, rutin acid	AST, ALP, ALT
Acacia catechu [30]	Khair	Fabaceae	seed	hydroxyl propyl cellulose	Ethanolic	Quercetin, catechin	AST, ALT, ALP, LDH
Bassia Latifolia [31]	Mohua	Sapotaceae	Bark	Carbon Tetrachloride, Alcohol and	Ethanolic		ALT, ALP, BILD, BILT, ALB, PRO,

				Ranitidine			CHO, TG,
Cordia obliqua [32]	Clammy cherry	Boraginaceae	Fruit	paracetamol	ethanolic and aqueous	Macrophylline, coumarins, β – sitosterol, quercetin, quercitrin	ALT, AST, ALP, direct bilirubin
Mallotus repandus [33]		Euphorbiaceae	Stem	D-Galactosamine	Ethyl Acetate	α-humulene, β-Selinene, Aciphyllene, α-copaen, caryophyllene oxide	ALT, AST, ALP, direct bilirubin, Total protein
Dipteracanthus patulus [34]	Spreading Ruellia	Acanthaceae	Whole plant	Paracetamol	Ethyl acetate	Vanilloside, Acteoside, Syringin, Cistanoside E, Isoacteoside	SGOT, SGPT, ALP
Schrebera swietenioides [35]	Mala plasu	Oleaceae	Fruit	CCl_4	Ethanolic	Sitosterol, Gallic acid, Caffeic acid, Rutin, Apigenin-7-glucoside, Catechin, kaempferol	SGPT, SGOT, ALP and Total bilirubin
Barleria Cuspidata [36]	Spiny Barleria	Acanthaceae	Whole plant	CCl_4	Methanolic	Barlerinoside, barlerin, acetylbarlerin, lupulinoside	AST, ALP, ALT, ACP
Baliospermum montanum [37]	Willd Muell Arg	Euphorbiaceae	Root	Ethanol & CCl_4	Hydroalcoholic	Axillarenic acid, Baliospermin, Montanin	AST, ALT, Bilirubin
Acampe praemorsa [38]	Brittle orchid	Orchidaceae	Aerial parts	Ethanol	Hydro-alcoholic	Phenanthraquinone, Amoenylin, Isoamoenylin, Flavanthrin	ALT, AST, ALP, Total bilirubin, Total protein
Gardenia gummifera L.f. [39]	Gummy cape jasmine	Rubeaceae	Fruit	CCl_4	Methanolic	Furfural, Maltol, Pantanoic acid,	SGPT, SGOT, ALP, Total protein, Total bilirubin
Ehretia laevis Roxb [40]	Dant-Rang	Boraginaceae	Flowers	Paracetamol	Hydro-alcoholic	α and β amyrin, piperazine, Gallic acid, Tannic acid, Rutin, Decanoic acids, Phthalic acid, Phytol,	ASAT, ALAT, ALP, and Total Protein
Zanthoxylum armatum [41]	Suterberry	Rutaceae	Rhizome	Paracetamol	Ethyl acetate, Chloroform Methanol	Zanthonitrile, Armatamide, Berberine, Limonene, Linalool	AST, ALT, ALP, Total bilirubin, Total protein
Foeniculum vulgare [42]	Sweet fennel	Umbellifers	Seed	Paracetamol	Ethanolic	Anethole, Estragole, Fenchone, Limonene, Phellandrene, Pinene	AST, ALP, ALT, Bilirubin
Leucas cephalotes [43]	Head Leucas (Dronpushpi)	Lamiaceae	Whole plant	Paracetamol	Ethanolic	Oleanolic acid, Ursolic acid, 3-sitosterol, α &ß Sitosterol, Asperphenamate, Maslinic acid, Linifoliside, Nectandrin B	ALT, AST, ALP, Bilirubin
Olive Leaf [44]	Olea europaea	Oleaceae	leaves	CCl_4	Super Critical Carbon Dioxide	Oleuropein, Hydroxytyrosol, Luteolin, Rutin, Caffeic acid, Catechin	ALT, AST, ALP, LDH
Actiniopteris radiata [45]	Ray fern	Pteridaceae	Root	Paracetamol	Hexane, Ethyl acetate, Hydro-alcoholic	Hentriacontane, Hentriacontanol, β-sitosterol, Quercetin-3-rutinoside (Rutin), β-sitosterol palmitate	SGPT, SGOT, ALT, AST, ALP, Total bilirubin
Pentatropis nivalis [46]	White Milkweed	Apocynaceae	Aerial part	CCl_4	Methanol	Acokanthera, Apocynum, Cerbera, Nerium	SGPT, SGOT, ALP, Cholesterol, Total bilirubin
Bassia latifolia Roxb [47]	Butter Tree	Sapotaceae	Leaves, Fruit	Paracetamol	Ethanolic	Madhucic acid, Farnesol, α-Farnesene, Dendrolasin, 2,3-Dihydrofarnesol,	SGPT, SGOT, SALP, Total bilirubin, Direct bilirubin
Hibiscus surattensis [48]	Bush Sorrel	Malvaceae	Aerial parts	CCl_4	Ethyl acetate, Methanol	Kaempferol, Morin, Trifolin, Quercetin, Spiraeoside	ALT, AST, ALP, Total protein, Total bilirubin

Chenopodium album linn [49]	Goosefoot	Amaranthaceae	Leaves	Paracetamol	Methanolic	β-carotene, Catechin, Gallocatechin, Caffeic acid, p-Coumaric acid, Ferulic acid, β-sitosterol	SGOT, SGPT, ALP, Direct bilirubin, Total bilirubin
Moringa oleifera [50]	Drumstick tree	Moringaceae	Leaves	Paracetamol	Nil	Quercetin Astragalin, Kaempferol, Apegenin, Genistein, Epicatechin	ALT, AST, Gamma Glutamyl Transferase (GGT)

Conclusion

The numerous pharmacological qualities of therapeutic plants that have been examined experimentally were gathered in this study. However, it is critical to recognise and identify and describe the lead molecule produced from plants that may have the capacity to protect the liver. The hepatoprotective effects of medicinal plants may be due to their ability to reduce oxidative stress and modulate metabolic pathways that leads to hepatotoxicity. Medicinal plants that are high in phytochemicals have high antioxidant activity, which helps to prevent liver damage. These data could be used to justify additional research into the comprehensive pharmacological evaluation of hepatoprotective medicinal plants.

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