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INDIAN HERBS IN THE TREATMENT OF LIVER INJURY: A MECHANISM-BASED REVIEW

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ABSTRACT

Object: The current study aims to investigate Indian herbs as potential effective liver injury treatments. Liver damage is an inflammatory condition that affects the liver and can be caused by a variety of factors, including changes in lifestyle in both men and women. **Methods:** The liver is an essential organ that is involved in the metabolism and removal of foreign substances from the body. Liver damage by various toxic chemicals (such as certain antibiotics, chemotherapy drugs, carbon tetrachloride (CCl4), thioacetamide (TAA), and microorganisms) as well as excessive alcohol use cause liver cell injury. The important health issue of liver malfunction or injury presents difficulties for the pharmaceutical Industry, drug regulatory organizations, and healthcare practitioners. The synthetic medications used to treat liver diseases in this situation also induce liver damage. As a result, herbal medications are used widely and have gained popularity. For a very long time, herbal remedies have been utilized to heal liver ailments. **Results:** In the present work, the plants used in this investigation were categorized using a table that included information about each plant's particular part of plants, pharmacological activity, extraction solvents, dosage, animal choice, and the results of hepatoprotective studies. **Conclusion:** This study compiled the various herbal plant have hepatoprotective properties which have been studied experimentally. Medicinal plants have hepatoprotective properties due to their ability to reduce oxidative stress and modify metabolic pathways that are connected to hepatotoxicity. This review may provide for further studies on pharmacological evaluation of hepatoprotective medicinal plants in systematic manner.

KEYWORDS: Indian herbs, safety, active constituent, treatment, liver injury, hepatoprotective.

INTRODUCTION

The liver is the biggest and most complicated internal organ in living systems. It varied functions play a significant part in maintaining the interior environment (Maqbool M *et al.* 2019) These actions are related to a number of important functions, such as secretion, metabolism, and storage. Additionally, to synthesis this organ has the capacity to detoxify both endogenous (metabolic) both internal (waste) and external (toxic substances) poisons. The liver performs a variety of biochemical functions, including digestion, energy production, reproduction, nutrition, and growth. It supports bile secretion, vitamin synthesis, and the metabolism of carbohydrates and fats. Because of these functions, liver disease continues to be one of the major risks to public health and a major issue. Liver injury caused by toxic chemicals (e.g. carbon tetrachloride (CCl4), thioacetamide, dimethyl nitrosamine (DMN), D-galactosamine) and certain drugs (e.g. antibiotics, paracetamol, aspirin etc.) as well as microorganisms and autoimmune conditions (immune hepatitis and primary biliary cirrhosis). When the cells, tissues, structures, and activities of the liver are damaged, it is called liver disease (Alkandahri MY *et al.* 2023). In view of severe adverse side effects of synthetic agents, there is growing focus to develop more valuable and protected drugs which may raise the therapeutic benefits for patients. A large number of medicinal plants have been tested and found to contain active principles with therapeutic properties against hepatotoxicity (Gupta R *et al.* 2015). Plants contain a variety of chemical constituents like phenols, coumarins, lignans, essential oil, monoterpenes, carotenoids, glycosides, flavonoids, organic acids, lipids, alkaloids and xanthene which showed hepatoprotective activity (Bhawna S *et al.* 2009). Around 80% of patients with liver disease use herbal treatments because they are easy to find, have low toxicity, have pharmacological activity and 30% are prescribed by physicians (Alkandahri MY *et al.* 2023). Liver disease approximately 2 million deaths globally each year. 1 million due to cirrhosis- related problems and 1 million due to hepatocellular carcinoma and viral hepatitis. In India has reached 268,580 (3.17% of all deaths) annually (Asrani SK et al. 2019). In the conventional Indian medical system, mixed plant extracts and plant formulations are preferred above single drugs (Shakti D *et al.* 2011). The use of polyherbal formulations in the treatment of a wide range of disorders has gained great global attention in recent years. Rats with liver illnesses and abnormalities have responded well to polyherbal formulations (Walker Roger *et al.* 2012). This review article

has been presented to enumerate some indigenous plants that have hepatoprotective properties such as Andrographis Peniculata, Phyllanthus Niruri, Adhatoda Vasaca, Cichorium Intybus, Tecomella Undulata, Eclipta Alba was it.

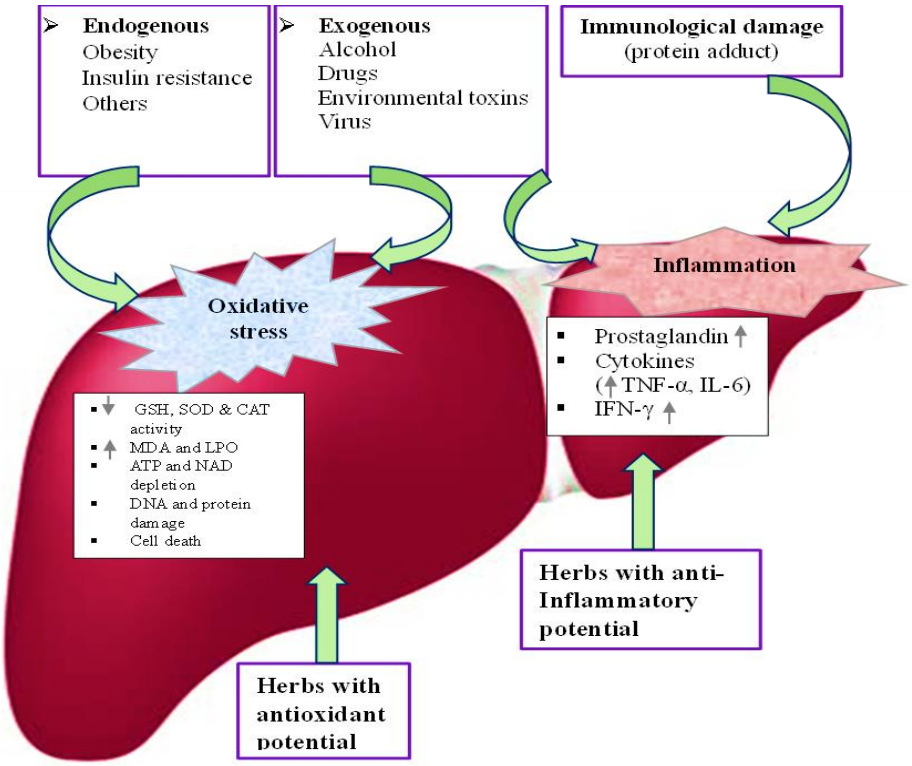

Fig. no. 1: Herbs and their mechanism of action for hepatoprotective activity.

HEPATOPROTECTIVE PLANTS

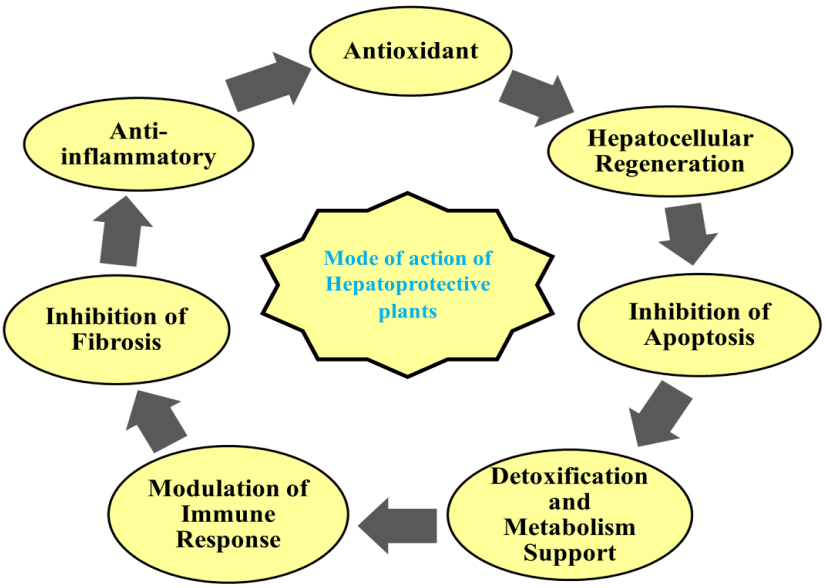

Fig. no. 2: The herbs show some modes of action for hepatoprotective.

1 Andrographis Peniculata

Andrographis paniculata Acanthaceae is the family *Acanthaceae*, also referred to as Kalmegh or the King of Bitters. *A. paniculata* contains lactones, diterpenes, and flavonoids. Although flavonoids can be separated from leaves, they are primarily found in roots. Kalmeghin and andrographolides, two bitter lactones, are present in the leaves. Around 10 flavonoids and 20 diterpenoids were extracted with ethanol or methanol from the entire plant, leaf, and stem of A. paniculata to produce active compounds such as andrographolide, isoandrographolide, neoandrographolide, and 14-Deoxy-11,12-didehydroandrographolide, and andrographiside. (Chao WW *et al.* 2012). The therapeutic effect is due to presence of diterpenoid lactone derivatives of *Andrographis paniculata* mainly andrographolide (Gonde DP *et al.* 2023).

Taxonomical Classification

Kingdom: Plantae

Division: Angiosperma

Class: Dicotyledonae

Order: Personales

Family: *Acanthaceae.*

Genus: Andrographis

Species: Paniculata

Fig. no. 3: Leaves of Andrographis Peniculata.

Table no. 1: List of few hepatoprotective *Andrographis paniculata* against toxic chemical induced liver damage in experimental animals.

SI No.	Part of plant	Solvent used	Dosing	Animal	Inducing agent	Outcome	Reference
1.	Aerial	Ethanolic extracts	100-200 mg/kg	Swiss albino mice	paracetamol	Reduced free radical in a concentration dependent manner	Nagalekshmi R *et al.*, 2011
2.	Leaves	Methanolic extracts	(low dose)10-100 mg/kg (high dose)	Albino mice	Paracetamol	Significantly reduced in both low and high doses of the *AP*	Sutha *et al.*, 2010
3.	Leaves	Ethanolic extracts	Non-toxic up to a level of 300 mg/kg	Wistar Albino Rats	CCl4	Prevents lipid peroxidation, and exhibits antioxidant effects	Ali S. K *et al.*, 2023
4.	Leaves	Aqueous extracts	100,200 and 300 mg/kg safe dose 3000 mg/kg	Wistar Albino Rats	CCl4	A significant decrease in hepatic tissue (GSH) glutathione in dose dependent manner	Nasir A. *et al.*, 2013
5.	Leaves	Aqueous extracts	250 and 500 mg/kg	Wistar Albino Rats	CCl4	Significant decrease biochemical parameter at different dose	Alasyam N. *et al.*, 2016

2 Phyllanthus Niruri

Phyllanthus niruri (family: Euphorbiaceae) locally known as 'Bhumi amlaki' Its taste is bitter. Niruri is a perennial herb distributed throughout India. Whole plant, fresh leaves and fruits are used to treat various ailments and leaf and fruit extracts showed antioxidant activity (Harish R *et al.* 2006). Several bioactive molecules, such as lignans, phyllanthin, hypophyllanthin, flavonoids, glycosides and tannins, have been reported in the extracts of *P. niruri* (*Sabir* SM *et al.* 2008). Phyllanthin and hypophyllanthin reported to reduce hepatotoxicity. Aqueous extract of P. niruri have a wide range of therapeutical activities such as hepatoprotective, anticancer, antioxidant, anti-inflammatory, lipid-lowering action and Methanolic extract of P. niruri exhibited immunomodulatory activity and anti-HIV activity (Hashem M *et al.* 2020).

Taxonomical Classification

Kingdom: Plantae

Phylum: Anthrophyta

Class: magnoliopsida (eudicotyledones)

Order: Euphorbiales

Family: Euphorbiaceae

Genus: phyllanthus

Species: niruri

Fig. no. 4: Whole plant of *Phyllanthus niruri.*

Table no. 2: List of few hepatoprotective *Phyllanthus niruri* against toxic chemical induced liver damage in experimental animals.

SI No.	Part of plant	Solvent used	Dosing	Animal	Inducing agent	Outcome	Reference
1.	Whole	Aqueous extracts	50 or 100 mg/kg	Swiss male albino mice	Nimesulide	Antioxidant, PN extract at a dose of 100 mg/kg was more effective than 50 mg/kg and IP is more effective than oral.	Chatterjee M., Sil P.C *et al.*, 2006
2.	Whole	Aqueous and methanolic extracts	100 mg/kg	Wistar albino rats	CCl4	Free radical scavenging, inhibition of ROS and lipid peroxidation.	Harish R. *et al.*, 2006
3.	Leaves	Aqueous extracts	100, 50 and 25 mg/kg Safe dose 2000 mg/kg	Male grower rabbits	Paracetamol	The best healing effect of P. Niruri administered at 25 mg/kg.	Makoshi M.S *et al.*, 2013
4.	Roots	Aqueous extracts	100 mg/ kg	Wistar albino rats	CCl4	Inhibited lipid peroxidation and improved the GSH and MDA status.	Manjrekar A P. *et al.*, 2008
5.	Whole	Ethanol extract	100 - 200 mg/kg no mortality doses up to 2 g/kg and 5 g/kg	Sprague Dawley rats	Thioacetamide	Treatment ultimately decreased liver to body weight ratio, which was closer to that of the controls.	Amin Z A. *et al.*, 2012

3 Adhatoda Vasaca

Adhatoda vasica Nees., belongs to the family of *Acanthaceae* is commonly known as Malabar nut, A famous Ayurvedic medicinal plant, which widely distributed in India (Shoaib A *et al.* 2021). Leaves and stems of the plant have been reported to contain an alkaloid mimosine, leaves also contain mucilage and root contains tannins (Vinothapooshan G *et al.* 2010). The extracts of the plant were prepared by using various solvent (alcohol, chloroform and ether) but they alcoholic extract showed a significant ($p<0.05$) protective effect on liver as compared with others. The presence of its biologically active constituents like Vasicinone, alkaloids, flavonoids, Deoxyvasicine, tannins, Vasicine, Vasicinol, Vasakin in the plant. The possible activity is due to the presence of the chemical constituent vasicinone (Shoaib A *et al.* 2021).

Taxonomical Classification

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Lamiales

Family: *Acanthaceae.*

Genus: *Adhatoda*

Species: *vasica*

Fig no. 5: Leaves of *Adhatoda vasica.*

Table no. 3: List of few hepatoprotective *Adhatoda vasica* against toxic chemical induced liver damage in experimental animals.

SI No.	Part of plant	Solvent used	Dosing	Animal	Inducing agent	Outcome	Reference
1.	Whole plant	Ethyl acetate	100 and 200mg/kg almost normalized these defects	Swiss albino male rats	CCl4	Preventing process of lipid per oxidation, cytochrome p-450 activity,	Ahmad R *et al.*, 2013
2.	Leaves	Methanol chloroform diethyl ether	200mg/kg 200mg/kg 200mg/kg Max. Safe dose 2000mg/kg	Wistar albino rats	CCl4	Methanolic extract of AV exhibited a hepato-protective compare to other two extracts	Vinothapooshan G, Sundar K *et al.*, 2010
3.	Leaves	Aqueous extracts	50 and 100 mg/kg	Wistar albino rats	D-galactosa amine	Lipid peroxidation and protein concentration in the liver were estimated.	Bhattacharyyaa D *et al.*, 2005
4.	Leaves	Aqueous extracts	250 mg/Kg and 500 mg/kg	Wistar albino rats	CCl4	The lowering of enzyme levels is a definite designation of hepatoprotective action of the drug	Kumar M *et al.*, 2015
5.	Leaves	Ethyl alcohol	200-400 mg/kg and safe dose 600 mg/kg	Swiss Albino mice	CCl4	Antioxidant character of vasicinone may be responsible for its hepatoprotective function.	Sarkara C *et al.*,2014

4 Cichorium Intybus

Cichorium intybus (Linn.) was also known as cichory belongs to family *Asteraceae*, in general, chicory is known as a popular coffee substitute (Matvieieva N *et al.* 2023). Leaves of *C. intybus* were found to have antioxidant properties. Leaves also have the ability to inhibit lipid peroxidation. The seeds of the Chicorium intybus are also reported to contain steroids, terpenoids, vitamin C and tannins (Akhtar MS *et al.* 2023). Several chemical constituents such as inulin, sesquiterpene lactones, cichoric acid, coumarins, vitamins and minerals, flavonoids are identified in different parts of the chicory plant. The main constituents of chicory reported to be present in the root are inulin, reducing sugars and sucrose. The water and methanolic extract of kasani have hepatoprotective role (Zafar R *et al.* 1998).

Taxonomical Classification

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Asterales

Family: *Asteraceae.*

Genus: *Cichorium*

Species: *intybus*

Fig no. 6: Whole plant of *Cichorium intybus L.*

Table no. 4: List of few hepatoprotective *Cichorium intybus* L. against toxic chemical induced liver damage in experimental animals.

SI No.	Part of plant	Solvent used	Dosing	Animal	Inducing agent	Outcome	Reference
1.	leaves	Hydroalcoholic extract	200, 400 and 500 mg/kg	Wistar albino rats	CCl4	Significance due to its membrane stabilizing effect on hepatic cells by the antioxidant effect of extract.	Heibatollah S *et al.*, 2008
2.	Whole	Methanol extract	250 and 500 mg/kg. safe dose up to 5 g/kg	Sprague Dawley rats	CCl4	Importance due to a membrane stabilizing effect, antioxidant	Atta A. H. *et al.*, 2010
3.	Leaves	Hydroalcoholic extract	50, 100, or 200 mg/kg	Sprague Dawley rats	CCl4	200 mg/kg did not protect rat liver because its toxic effect overcame its protective effect against CCl4.	Jamshidzadeha A *et al.*, 2006
4.	Roots	Alcoholic and aqueous extracts	400 mg/kg Safe dose 2000 mg/kg (2g/kg)	Wistar albino rats	CCl4	Significance due to the presence of flavonoids, gives hepatoprotective properties.	Nallamilli B R *et al.*, 2023

5 Tecomella Undulata

Tecomella undulata (Bignoniaceae), is a locally known as Rohida, found in Thar Desert regions of northwest and Western India (Singh D *et al.* 2011). various chemicals, including radermachol, lapachol, tecomaquinone-I, α-lapachone, β-lapachone, stigmasterol, β-sitosterol, oleanolic acid, ursolic acid, tecmine, luteol, β-Sitosterol, flavonoids, tannins, coumarins, and betulinic acid, have been isolated from plant components, mainly the bark and leaves. (Dhir R *et al.* 2012). Experimentally, the whole plant showed analgesic and anti-inflammatory activity and the stem bark with other herbal formulations offered a hepatoprotective activity (Singh D *et al.* 2011). It has been used in the indigenous systems of medicine for liver, spleen and abdominal complaints (Khatri A *et al.* 2009).

Taxonomical Classification

Kingdom: Plantae

Phylum: Tracheophyta

Class: Magnoliopsida

Order: Lamiales

Family: *Bignoniaceae*

Genus: *Tecomella*

Species: *undulate*

Fig no. 7: Plant of *Tecomella undulate.*

Table no. 5: List of few hepatoprotective *Tecomella undulata* against toxic chemical induced liver damage in experimental animals.

SI No.	Part of plant	Solvent used	Dosing	Animal	Inducing agent	Outcome	Reference
1.	Leaves	Methanol extract	100 and 200 mg /kg Safe dose 4 g/kg(4000mg)	Wistar albino male	Alcohol and Paracetamol	Antioxidant activity of T. Undulata might be due to the presence of flavonoids, quinones	Singh D *et al.*, 2011
2.	Bark	Ethanolic extracts	100, 150 and 200 mg/kg Safe up to dose of 2000 mg/kg	Albino mice and Wistar rats	Paracetamol	Significance due to its free radical-scavenging and antioxidant activity.	Pateli K N. *et al.*, 2011
3.	Bark	Methanolic extract	200 mg/kg Safe up to2000 mg/kg.	Wistar albino rats	CCl4	It maybe hypothesized that flavonoids present it responsible for the hepatoprotective.	Rana M.G. *et al.*, 2008
4	Bark	Methanolic extract	200 or 400 mg/kg no mortality 5000 mg/kg	Wistar albino rats	CCl4	Hepatoprotective activity due to the partially presence of betulinic acid.	Jain M *et al.*, 2012

6 Eclipta Alba

Eclipta alba (L.) commonly known as bhringraj in Sanskrit as well as false daisy in English, is a species of plant in the family *Asteraceae*. The leaves contain stigmasterol, β terthienylmethanol, wedelolactone, demethylwedelolactone and demethylwedelolactone-7-glucoside. The roots give hentriacontanol and heptacosanol, Stigmasterol, Ecliptal. The aerial part contains phytosterol, β-amyrin in the n-hexane extract and luteolin-7-glucoside, β-glucoside of phytosterol, a glucoside of a triterpenic acid and wedelolactone. The Stems give Wedelolactone and Seeds Sterols (Bhalerao SA *et al.* 2013, Jadhav VM *et al.* 2009). Coumestans (wedelolactone and demethylwedelolactone), ecliptal, beta-amyrin, stigmasterol and sitosterol, ecliptasaponin a and b, polyacetylenes, phyllanthin and hypophyllanthin, flavonoids have been mentioned as the possible components behind the protective effect on liver as well as against liver disorders. Solvent such as ethanol, methanol, alcohol, and aqueous, chloroform is used (Jahan R *et al.* 2014).

Taxonomical Classification

Kingdom: Plantae

Division: Tracheophyta

Class: Magnoliopsida

Order: Lamiales

Family: Asteraceae

Genus: *Eclipta*

Species: *Alba*

Fig. no. 8: Leaves of *Eclipta alba* L.

Table no. 6 List of few hepatoprotective *Eclipta alba* L. against toxic chemical induced liver damage in experimental animals.

SI No.	Part of plant	Solvent used	Dosing	Animal	Inducing agent	Outcome	Reference
1.	Leaves	Ethanolic extracts	10, 30, 100, 300 and 1000 mg/kg	Charles fosters rats and Swiss albino mice	CCl4	Showed dose dependent reduction of CC14 induced values of these Parameters.	Singh B. *et al.*, 2001
2.	Leaves	Ethanolic extracts	200 mg/kg	Wistar albino rats	Alcohol	Significant dose dependent hepatoprotective activity.	K Arun *et al.*, 2011
3.	Leaves	Ethanolic extracts	200, 250 and 300 mg/kg	Albino Wistar rats	CCl4	Callus extract (20 mg) produced a higher cardiac inhibitory activity than that of leaf extracts (20 mg).	Zafar R, Sagar BP *et al.*, 2000
4.	Leaves	Ethanolic extracts	200mg/kg	Wistar albino rats	Sodium arsenite	Ethanol leaf extract of *Eclipta alba* exhibited some potential protective effect and can probably suppress.	A Oyeronke *et al.*, 2021

CONCLUSION

The several herbal plants included in this study have been shown to have hepatoprotective qualities through experimental research. Because they can alter metabolic pathways linked to hepatotoxicity and lower oxidative stress, medicinal herbs offer hepatoprotective qualities. Its plant has a unique class of phytochemical constituents called flavonoids and phenols, which exhibit strong antioxidant properties and alleviate liver injury. Consequently, to create potent

Indian medicinal plant compositions by appropriate pharmacological testing. These findings could support more research on the comprehensive pharmacological assessment of hepatoprotective medicinal plants.

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Conflict of interest

The author declares no conflict of interest.

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