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Review Article

Indigenous Wisdom of Ayurvedic Drugs to Treat Liver Disorders-Review Article

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Abstract: The liver, a vital organ in the body, synthesizes hormones, decomposes RBC in the blood, and regulates glycogen storage. The liver also performs detoxification and is the primary site for drug metabolism. Therefore, hepatoprotective medications are necessary to keep the liver in good health. *Ayurvedic* drugs are widely used as hepatoprotective agents. The study aims to review the *Yakrit* (liver) concept in Ayurvedic literature, identify hepatoprotective plants from classical Ayurveda texts, and understand their mode of action on the liver based on existing scientific evidence. The classical Ayurveda literature and electronic databases such as Google Scholar, PubMed, Web of Science, and ARP were searched until October 2022 to find relevant studies using MESH terms. The search of classical Ayurveda texts showed several herbal sources that are advocated for use in liver disorders. The in vivo studies for these plants showed that seven protected the liver from CCl4-induced hepatic damage. Furthermore, the levels of liver enzymes were reduced, and there was evidence of reversal of fatty changes in the liver in mice fed with a high-fat diet. One of the essential organs that aid in sustaining bodily health is the liver. Some plants have been endowed by nature with the ability to treat, prevent, and cure liver disorders while causing fewer negative effects. Herb-based Ayurveda drugs can be a potent source of hepatoprotective agents, though detailed studies need to be conducted to generate more substantial evidence.

Keywords: Traditional Medicine, Herbal Drugs, Liver, *Yakrit*, Hepato-Protective, Medicinal Plants.

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1. INTRODUCTION

Ayurvedic drugs are widely used in the treatment of various disorders and diseases. The liver is a reddish brown, wedge-shaped solid organ and the largest gland present in the body. It mainly removes various toxic substances from the human body's blood supply. Hepatoprotective drugs protect the liver, an important organ in the body. It removes toxic substances from the blood supply and regulates metabolic activities. The liver is also involved in producing hormones, decomposition of RBC in the blood, and regulating glycogen storage; hepatoprotective medications are necessary since the liver needs to be protected. The nutritional level of a person is influenced by both what they consume and what their liver processes, making the liver crucial. It is surprising and incredible that basic plant remedies might have something to contribute, given how complicated the chemistry of the liver is and how important it is to human physiology. One of the essential organs, the liver, serves as a hub for metabolizing nutrients like carbohydrates, lipids, and protein. It also performs the function of detoxification in the body. The chemicals, like dietary preservatives or medications, are metabolized in the liver. Additionally, it regulates the body's metabolism and excretion of medicines and other xenobiotics, detoxifying and removing them to guard against foreign chemicals. Ancient Ayurveda texts provide a thorough insight into a vast number of medicines. These medicines are based either on plant sources, mineral sources, or a combination of both. Ayurveda drugs, mainly plant-based medications, are widely used as hepatoprotective agents. Moreover, being in use for centuries, these medicines offer abundant clinical data for their effectiveness. However, most of this data is undocumented. Recently, many in vivo and in vitro studies have been conducted to evaluate their efficacy on liver diseases of varied etiologies. The current study aims to review the information from research published on potential phytochemicals extracted from herbal plants tested in hepatotoxicity models.

1.1 Description of Liver and its disorders in Ayurveda

Since the Vedic civilization, the liver has been regarded in *Ayurvedic* literature as an important *anga (organ)* of the human body. According to *Bhavamishra* (c. 16th Century), it is located just beneath the *hridaya* (heart) and serves as the *pitta* and *shonitha* (blood) *sthana*[1] *Susrutha*, the residence of *Ranjaka Pitta* (500 BC)[2] *Susrutha* refers to *Yakrit (liver*) as the "place of blood" (500 BC)[3] ~~[3]~~ In his discussion of the *srotas* (body channels), *Charaka* (around 1000 BC)referred to the *yakrit* (liver) and *pleeha* (spleen)as the *moola* (root) of the *raktavaha Srotas* (blood transporting channels)[4] However, the phrase "yakrit vikara" was first used by Bhavamisra (liver disorders). Madhavanidana categorizes yakrit roga (liver disease) as a separate element in parishista prakarana[5]. The etiopathogenesis of Yakrit roga is depicted in Figure 1. Enhancing liver detoxification mechanisms and aiding in liver damage prevention are the main objectives while treating liver issues. Unfortunately, modern therapies lack effective and secure hepatoprotective drugs. The development of plant-based hepatoprotective medications that are effective against a range of liver illnesses has therefore received the proper attention on a global scale. The term *"yakritvikara,"* which refers to liver ailments, was first used by the *Bhavamishra*. The first step in treating liver illnesses, such as *yakrit*, is to begin the detoxification process, cleanse the liver, and guard against additional harm. *Ayurvedic* medicines have gained relevance worldwide for treating liver disorders and preventing liver illnesses because modern medicine lacks hepato-protective pharmaceuticals. The liver also works to break down and eliminate other harmful substances that could harm the organ or impair its functionality.

Fig 1: *Yakrit Roga's* pathophysiology and etiology (liver disease)

The study aims to review the available scientific literature and classical Ayurveda texts to search for effective

hepatoprotective *Ayurvedic* herbal medications. An attempt is also made to understand their mechanism of action in treating Liver Disorders.

2. MATERIALS AND METHODS

The classical Ayurveda texts namely Charak Samhita, Sushruta Samhita, Astanga Hridaya, , Madhav Nidana, Sharangdhara Samhita, and Bhavprakashwere searched, and hepatoprotective drugs were enlisted initially. Later, these drugs were looked up in the electronic databases Google Scholar, PubMed, Web of Science, and ARP for relevant animal studies up to October 2022. All the references were reviewed, compiled, analyzed, and discussed thoroughly to understand the concept of liver and treatment in hepatoprotective disorders.

3. RESULT

Several Ayurvedic medications include plant components that shield the liver from harm. A few medicines or herbal plants also enhance liver functions. Table 1 shows several herbs along with their *Rasapanchaka*[6]. Most drugs with hepatoprotective actions have mainly *Katu, Tikta,* and *Kashaya Rasa*. The main properties of these drugs are *Guru (quality), Snigdha (unctuous), Laghu (easily digested), Ruksha (dry), and Teekshan.* Figure -2 shows herbal sources possessing hepatoprotective properties

Table no. 1: Properties of Hepatoprotective drug

S.N	Plant	Rasa	Guna	Virya	Vipaka	Doshakarma
1.	***Pippali*** [Piper longum]	*Katu*	*Laghu,Snigdha, Tikshna*	*Ushna*	*Madhura*	Act on all three *doshas.*
2.	***Katuki*** [Picrorhiza kuro]	*Tikta*	*Laghu,Ruksha*	*Sheeta*	*Katu*	*Kaphapittahara*
3.	***Guduchi*** [Tinospora cordifolia]	*Tikta, Kashaya*	*Guru,Snigdha*	*Ushna*	*Madhura*	*Tridoshahara*
4.	***Kalamegha*** [Andrographis paniculate]	*Tikta*	*Laghu,Ruksha*	*Ushna*	*Katu*	*Kaphapittahara*
5.	***Bhirngaraja*** [Eliptica alba]	*Tikta,Kashay*	*Laghu,Ruksha*	*Ushna*	*Katu*	*Kaphavatahara*
6.	***Daruharidra*** [Berberis aristate]	*Tikta, Kashay*	*Laghu,Ruksha*	*Ushna*	*Katu*	*Kaphapittahara*
7.	***Rohitaka*** [Techomaundulata]	*Katu,Tikta,Kashay*	*Laghu,Ruksha*	*Sheeta*	*Katu*	*Kaphapittahara*

Katu, Tikta, and Kashaya are the three flavors that makeup [Rasa (taste)] (astringent), Guru (quality), Snigdha (unctuous), Laghu (easily digested), Ruksha (dry), and Teeksha are tough to digest (sharp) Seeta (cool), Ushna, and Virya (potency) (hot) Vipaka (post metabolic impact) (post metabolic effect) Dosa karma (effect on functioning bodily entities)]

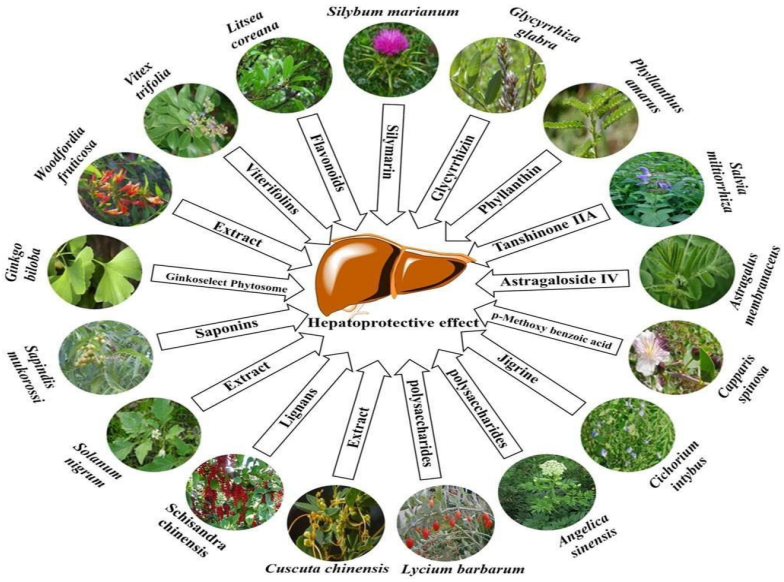

Fig2. Important medicinal plants and the compounds in them that are linked to hepatoprotective qualities[7]

3.1 The description of these drugs in context with the liver and their role in protecting the liver.

1.3.1 Pippali

A typical dietary spice used in India, Piper longum Linn., a member of the Piperaceae family, has been demonstrated to have numerous therapeutic benefits. It has been claimed to have immunomodulatory, anti-inflammatory, hepatoprotective, anti-asthmatic, and anti-inflammatory properties. It contains several alkaloids, including piperine, piperlongumine, and piperlonguminine, that aid in the regeneration of hepatocytes[8]. According to a study by Jagruti and Urvi[9], milk extract treatment in CCl4 caused liver damage but also had a substantial hepatoprotective effect on Piper longum Linn. Serum enzyme levels, total bilirubin, and direct

bilirubin all decreased. Hepatocytes were protected by Piper longum Linn. milk extract from CCl4-induced damage, according to histo-pathological observations. Slight fatty changes in the hepatic parenchymal cells further supported the variations in hepatic enzyme levels. It also showed liver cells that were healing around the necrotic region. The primary phytoconstituents in *pippali* affect the liver's SGOT, SGPT, and bilirubin levels (conjugated and unconjugated bilirubin). It normalizes the raised and lowered levels of direct and conjugated bilirubin and the elevated bilirubin level. It also demonstrates a positive impact on liver antioxidant activity. Additionally, it demonstrates its beneficial effects on the regeneration of liver cells near the necrotic area. Depending on the fruit, it acts as an aphrodisiac, digestive aid, carminative, stimulant, and appetizer. Its root works well as a stimulant. It is therapeutically provided when treating colic disease, vomiting, coughing, fever, worm infections, tumors, and burning feelings.

1.3.2 Katuki

The Ayurvedic medical system has traditionally utilized the well-known herb Picrorhiza kurroa Royle ex Benth. to treat fevers, dyspepsia, persistent diarrhea, scorpion stings, liver and upper respiratory tract ailments, and dyspepsia—the active ingredient in Picrorhiza kurroa Royle ex. Benth, kut kin, comprises iridoid glycosides such as picrosides I, II, and III and outside [10.] Picrorhiza kurroa Royle ex Benth's capacity to suppress the production of oxygen anions and scavenge free radicals may be responsible for its hepatoprotective effects. It has been demonstrated that picrorhiza, superoxide dismutase, metal-ion chelators, and xanthine oxidase inhibitors have similar antioxidant properties. The active components in picrorhiza have been shown in animal studies to have significant anti-cholestatic capabilities, and they seem to be even more powerful than silymarin against several liver-toxic medications[11] Additionally, Picrorhiza displays a dose-dependent choleretic action as shown by a rise in bile flow and bile salts and acids[12]

1.3.3 Guduchi

Guduchi is also referred to as Amrita or Tinospora cordifolia (Willd.) Miers. It is one of the most priceless medicinal plants used in Ayurveda. This herb is known by the name "*Amrita*" because of its capacity to bestow youth, energy, and longevity upon its use. It is well known for its hepatoprotective, adaptogenic, immuno-modulatory, and anti-fibrinolytic properties in contemporary medicine. Tinosporin's active component13 treats immune suppression caused by impaired liver function. Kupffer cells play a significant role in how liver damage develops. The carbon clearance test was used to assess Tinospora cordifolia (Willd.) Miers' impact on Kupffer cell performance. In albino rats exposed to carbon tetrachloride intoxication, the antihepatotoxic effects of Tinospora cordifolia (Willd.) were examined (CCl4). Exams for morphology, biochemistry (SGPT, SGOT, serum alkaline phosphatase, and serum bilirubin), and function (pentobarbitone sleep duration) were used to evaluate the liver. Nagarkatti et al. (1994) conducted research on Tinospora cordifolia (Willd.) Miers and discovered that it dramatically reduced CCl4-induced rat fibrosis and improved impaired Kupffer cell function in another rat model of chronic liver damage brought on by heterologous serum. It demonstrates that Tinospora cordifolia's anti-fibrotic actions may be brought on through stimulating kupffer cells [14]

1.3.4 Kalamegha

Asia has used the ancient Indian herb Andrographis paniculata Nees for millennia due to its effects on a variety of biological processes and disorders, from degenerative diseases to the common cold. The herb is referred to as the King of Bitters. It identifies and extracts the extremely bitter active component andrographolide from Andrographis paniculata Nees [15]. Using isolated rat hepatocytes produced ex vivo, research by Visen et al. (1993) on andrographolide demonstrated a strong dose-dependent protective effect against paracetamol-induced damage. Carrying out the trypan blue exclusion and oxygen absorption experiments greatly raised the percentage of hepatocytes that were viable. In serum and isolated liver cells, specific enzymes (GOT, GPT, and alkaline phosphatase) were guarded against the negative effects of paracetamol [16]. The bioactive component mitigates the negative effects of CCl4 and acetaminophen on certain blood enzymes and isolated hepatic cells (GOT, GPT, and alkaline phosphates). The findings showed that the plant extract has a choleretic impact that lowers cholestasis, lessens retention, and increases the liver's elimination of harmful xenobiotics. Additionally, it prompted the immune system to combat inflammation through the production of cytokinin from immunomodulators [17] Andrographolide, a diterpene lactone that is colorless, crystalline, and has a bitter taste, is one of the phytochemical components found in the aerial parts of Andrographis paniculata[18] It has been claimed that Andrographis paniculata's chemical components help gall bladder health. Function intensified biliary flow and was discovered to protect the liver. It exhibits an anti-diabetic effect, too [19]

1.3.5 Bhringaraja

The plant Eclipta alba Hassk also called *Bhringraja* is a member of the Asteraceae family. The leaf extract is revered in ayurveda medicine as a potent liver tonic. It is used to treat cirrhosis and hepatitis and has a wide spectrum of biological actions [20] The entire plant extract of Eclipta alba Hassk. It demonstrated protective efficacy against CCl4-induced liver damage in a 2008 study by Murugaian P et al. Ecliptine, an alkaloid found in the plant, has choleretic properties. The fact that the extract increased bile flow in rats suggests that it stimulated the liver's ability to release bile [21]

1.3.6 Daruharidra

Being a significant medicinal plant, Berberis asiatica DC. is widely used to cure several illnesses such as eye infections, skin conditions, jaundice, and rheumatism[22] According to reports, berberine, the plant's main alkaloid, has antioxidant properties 23 because of its capacity to contain antioxidants, Berberis aristata DC. Roots have more potent hepatoprotective effects against CCl4 intoxication in rats.

Significantly more serum and liver lipid peroxides were produced after acute CCl4 treatment. Treatment with berberine might lower these high levels. After the CCl4 injection, pathological examination revealed degeneration and necrosis. Treatment with berberine might reduce these effects to some degree[23]. Historically, wounds, diabetes, inflammations, and jaundice have all been treated with B. aristate's roots, stems, leaves, and fruits [24-26] This alkaloid's therapeutic effectiveness against neurological and cardiovascular disorders, amoebiasis, severe diarrhea, and cholera has been shown in clinical studies [27-29]

1.3.7 Rohitaka

A tropical coastal shrub with a height of up to 1 m, trachoma undulata G. Don. It happens all over the Indian subcontinent. Rats with albinism had their livers damaged in tests using leaves from Techoma undulata G. Don. Raised levels of marker enzymes such SGOT, SGPT, and total bilirubin accompanied the loss of membrane structure and integrity caused by lipid peroxidation. It reveals that membrane maintenance is a function of the plant. Techoma undulata G. Don Extract might have anti-oxidant properties that lessen the effects of ethanol on membrane lipid peroxidation and maintain membrane structure. The extract's inclusion of glycosides, flavonoids, proteins, amino acids, tannins, saponins, and triterpenoids may be the reason for this [30] The plant has analgesic and anti-inflammatory properties. In contrast, the stem bark has hepatoprotective properties. The plant has analgesic and anti-inflammatory properties, while the stem bark has hepatoprotective properties [31] properties, while the stem bark has hepatoprotective properties [32] While managing liver disorders, the main objectives are to improve functions, enhance detoxification mechanisms, and prevent further liver damage. Unfortunately, modern therapies lack effective and secure hepatoprotective drugs. The development of plant-based hepatoprotective medications that are effective against a range of liver illnesses has therefore received much attention on a global scale [33-36]**.** *Yakrit* (liver) is the seat of *rakta dhatu* (blood tissue), *pitta dosha* (a functional component of the body), and *Agni* (power of digestion). *Pitta dosha* is the primary focus of treatment for all liver illnesses in Ayurveda rather than the organ itself. The majority of hepatoprotective medications are *kapha pittashamaka* (pacifies *pitta*&*kapha* entities) [37-38]. All sorts of liver illnesses are frequently treated with the medications and foods that normalize *pitta*. Most hepatoprotective plants have *deepana- pachanga* karma and *Tikta- Katu rasa*, which is bitter and pungent tastes, respectively (digestive stimulant and carminative). These medicines primarily affect the digestive fire (*jatharagni*), the *dhatwagni*, and the *agni vardhaka* (increases fire entity in the body) systems (fire residing in tissues). Since these rasas (tastes) can speed up metabolism, these herbs assist in the digestion of nitrogenous waste products produced in the body due to disordered metabolism (mostly by promoting catabolism). The majority of hepatoprotective plants have *laghu* (easily digestible) and *ruksha*(dry) *gunas* (quality). Because they are quickly digestible and produce fewer nitrogenous waste products, *laghu guna* (quality of easy digestion) contributes to an increase in *jatharagni* (digestive fire). Because *ushna virya* (hot potency) boosts metabolism, it aids in boosting the *Jatharagni* (digestive fire) and *Dhatwagni* (catabolism)[39-40] Modern pharmacology suggests that the primary mechanism for liver protection may be related to the potent ability of hepatoprotective medications to increase levels of both enzymatic and non-enzymatic antioxidants while reducing intracellular levels of reactive oxygen species. These medications shield the liver's tissues from oxidative damage and, in some way, assist in promoting the liver's natural repair process [41-42.] Each hepatoprotective herb works differently. G. Techoma undulata Don can stabilize the hepatocyte membrane, preventing toxins from entering the cell via entero-hepatic recirculation. Tephrosa purpurea Pers., Berberis aristata DC, and Piper longum Linn.Linn's assistance in liver cell regeneration. aid in regenerating liver cells by enhancing the synthesis of ribosomal proteins and nuclear polymerase A. (Willd.) Miers' Tinospora cordifolia, the body's immune system is activated and immuno-modulated by molecules like interleukins and tumor necrosis factors produced by the Kuffer cells, which should be more active—boosting ribosomal protein synthesis and nuclear polymerase. Phyllanthus niruri Linn. has antiviral properties and aids in the activation or inhibition of microsomal activity. The plant Boerhavia diffusa Linn has antifibrinolytic properties. Andrographis paniculata Nees., Picrorhiza kurroa Royle ex Benth., and Eclipta alba Hassk. have shown significant choleretic activity[43.] Studies have shown that some herbs work well to heal liver issues. He has also been successfully treated with a few *Ayurvedic* chemical formulations listed in the *Sharangadhara Samhitha* (13th Century), such as *Phalatrikadi kwatha[44]*, *Vasa guduchyadi kashaya45, Patola katurohinyadi kashaya, Guda pippali[46], Arogyavardhini vati[47],* and *Rohitakarista[48]*.

4. CONCLUSION

The liver is the main organ involved in metabolism of both food and medicine in the body. A diseased liver shall not perform its function correctly, leading to impaired metabolism. Herbal drugs possess properties that can heal and enhance the functioning of a diseased liver in its primary stages. They can strengthen and cure the liver, which helps to restore its natural activities. Detailed studies must be undertaken to understand these herbs' underlying mechanism of action on hepatic cells.

5. AUTHOR CONTRIBUTION STATEMENT

Devanshi Maheshwari conceptualized and gathered the data about this work. Aditi provided valuable input in designing the manuscript. Bharat Rathi and Renu Rathi discussed the methodology and analyzed the data. All authors read and approved the final version of the manuscript.

6. CONFLICT OF INTEREST

Conflict of interest declared none.

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