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Hepatoprotective activity of medicinal plants in Indian folk medicine

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ABSTRACT
In Indian traditional medicine, a number of drug combinations are frequently employed as liver tonics. In this review, we have introduced various medicinal plants that are utilised mostly for the treatment of liver problems in Indian folk medicine, with focus on their hepatoprotective activities specifically against CC14 agent. In this investigation, articles were sought for using internet resources such as Web of Science, Scopus, and Science Direct. Search terms consisted of medicinal plants, traditional medicine, folk medicine, hepatoprotective,therapeutic applications, antioxidant, CC14, and antihepatotoxic, hepatitis, alone or in combination.AgeratumConyzoides, AlchemillaMollis, EuphorbiaTirucalliL.,AquilariaAgallocha are a few of the medicinal plants that have been employed in Indian folk medicine to treat liver diseases.Silymarin, phyllanthin, andrographolide, curcumin, picroside, hypophyllanthin, kutkoside, and glycyrrhizin are a few leads found in plants that may contain hepatoprotective agents. These compounds have also been shown to have strong hepatoprotective properties.
Keywords: Liver, Detoxification, Liver illnesses, Plant extracts

I. INTRODUCTION:

Medicinal plants are important to the provision of healthcare for people. Almost 80% of people worldwide utilise traditional medicine, which is largely composed of plant ingredients [1].Traditional medicine encompasses a wide spectrum of age-old, all-natural health care philosophies, including Ayurveda, Siddha, Amchi, Unani, and folk/tribal traditions. These medicinal practises date back to the beginning of time and have gradually evolved mostly based on practical experiences and little to no reference to contemporary scientific ideas.

These customs were transmitted down by oral tradition and/or restricted literacy, and they included prehistoric beliefs. Although herbal remedies are beneficial in treating a variety of conditions, they are frequently misused or exploited without sufficient science. Hence, in the context of contemporary science, these plant medications merit in-depth research.

In India's primarily rural and tribal regions, there are thought to be 7,500 plants utilised in traditional medicine. Of of these, the general public is either unaware of or has limited knowledge of the true medical benefits of more than 4,000 plants. Over 1,200 plants are used in the 1,200 or more traditional medical systems, including Ayurveda, Siddha, Amchi, Unani, and Tibetan [2].The development of priceless plant medicines for a variety of terrible diseases can be facilitated by thorough research into and documentation of plants utilised in regional medical traditions, as well as by pharmacological examination of these plants and their taxonomical relations. Random plant screening has not proven to be economically advantageous[3].

LIVER AILMENTS

The liver is crucial in the control of numerous physiological functions. It participates in a number of crucial processes, including metabolism, secretion, and storage. Several xenobiotics and pharmaceuticals can be detoxified in the liver. The digestive process is guided by the liver's bile acid along with a few other factors. One of the serious illnesses is liver disease.It can be divided into three categories: cirrhosis (which leads to liver fibrosis), hepatisis, and chronic or acute (inflammatory sickness) (non-inflammatory ailment). They are mostly brought on by a number of risk factors that create oxidative stress in the liver, which in turn causes peroxidation of lipids and other oxidative damages to the liver cells. Hepatitis and cirrhosis may be caused by increased lipid peroxidation during the metabolism of microsomal ethanol in the liver[4].

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LIVER CANCER RISK FACTORS

The common component revealed to be the cause of liver cirrhosis is chronic infection with the Hepatitis C and B virus [5]. The use of contaminated needles and the sharing of blood are two ways that the hepatitis C and B viruses can spread from one person to another. Prior to blood transfusion, a blood test can be used to lower this risk of transmission [6].Abuse of alcohol, which results in liver cirrhosis and hepatic cancer, is another risk factor [7]. Smoking, being overweight, having diabetes, and using tobacco all increase the risk of developing liver cancer [8].Certain types of liver cancer may increase your risk of developing if you are exposed to heavy metals through your drinking water [9]. Moreover, prolonged exposure to thorium dioxide (an X-ray compound), vinyl chloride, and aflatoxin can increase a person's risk of developing cirrhosis and liver cancer [10].

HEPATOPROTECTIVE PLANTS

Several medicinal plants have undergone testing and been found to contain active ingredients that have the ability to treat various illnesses. A variety of chemical components, including phenols, coumarins, lignans, essential oils, monoterpenes, carotenoids, glycosides, flavonoids, organic acids, lipids, alkaloids, and xanthines, are present in liver-protective plants.The development of completely plant-based hepatoprotective medications has therefore gained significance in the worldwide market because a wide variety of plants and formulations have been claimed to have hepatoprotective effects [11].

AGERATUM CONYZOIDES

Ageratum conyzoides is a member of the Eupatoriae tribe of the Asteraceae family. Ageratum's name comes from the Greek word a geras, which means "non-aging" and alludes to the longevity of the entire plant. On the other side, Conyzoides is derived from "konyz," the Greek name of the plant, which resembles Inula helenium. The bulk of the family's plants are herbaceous, while trees and shrubs are very uncommon.The tropical plant A. conyzoides is widespread in West Africa, as well as in some regions of Asia and South America. It is a perennial herb with branches that reaches a height of about 1 m. The plant flourishes in any garden soil, grows readily next to human settlement, and is widespread in waste areas and on abandoned buildings. Its moniker, "goat weed" or "billy goat weed," refers to its unique stench, which is likened in Australia to that of a male goat [12–14].

ANDROGRAPHIS PANICULATA

Argyrospermumpaniculatum (Burm. F.) Nees, a member of the Acanthaceae family, is the most widely used traditional medicinal plant used to treat a variety of illnesses such viral fever, chicken pox, not uncommon bloodless, diarrhoea,pharyngolaryngitis, eczema, herpes zoster, mumps, ulcer, neurodermatitis, infection, epidemic encephalitis B, and respiratory infections [15]. In countries like India, China, and Hongkong, the herb is frequently used as a traditional treatment for bites [15,16].Due to its well-known medicinal benefits, it is generally known as Kalmegh or the King of Bitters and is grown in several South Asian nations [17]. A. paniculata is frequently combined with other herbs and care items in the Ayurvedic medical system to treat patients with a variety of physical and mental conditions. It has been hypothesised that A. paniculata has been used for a long time in Indian medical systems to treat patients with liver diseases. [18] A. paniculata was tested for hepato renal shielding effect against ethanol-induced toxicity in mice, in addition to being utilised as a single drug to treat liver injury [19]. Mice were given an intraperitoneal pretreatment with androgaholides (500 mg/kg body weight) and arabinogalactan (125 mg/kg body weight) for 7 days prior to receiving an ethanol injection (7.5 mg/kg body weight). Compared to the ethanol-treated group, there was less toxicity, as determined by a special enzyme assay in the liver and kidney tissues, which also comprehensively measured andrograholides and arabinogalactan (a.k.a. Silymarin) [20].

ALCHEMILLA MOLLIS

Alchemilla mollis (Buser) (Rosaceae Family) Traditional European medicine also makes use of Rothm, a plant of to the genus Alchemilla. A. mollis extract is used in the commercial drug "HerbaAlchemillae," which has astringent, diuretic, and antispasmodic properties. Folk medicine also uses it to treat excessive menstruation and wounds. [21-23]Especially in northern and northern-eastern Anatolia, A. mollis grows naturally and extensively in Turkey. [24] The Alchemilla mollis The hepatoprotective efficacy of Rothm aerial component and root methanolic-water extracts on carbon tetrachloride caused hepatotoxicity and the hypoglycemic activity on alloxan-induced diabetic

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mice were assessed. None of the examined extracts had any impact on blood sugar levels.None of the examined extracts had any impact on blood sugar levels. Nevertheless, serum ALT levels were dramatically decreased by both the aerial portion and root extracts at doses of 100 mg/kg and 200 mg/kg, according to hepatoprotective activity data.When compared to the carbon tetrachloride group, A. mollis aerial part extracts at a dose of 200 mg/kg showed the most significant activity in terms of inducing recovery from cellular damage, according to histopathological analysis. There is proof that A. mollis' phenolic content, particularly flavonoids, which have strong antioxidant properties, has a hepatoprotective effect on the body. [25]

GARDENIA GUMMIFERA LINN

In Indian traditional medicine, Gardenia gummifera (Rubiaceae) is well-known for its therapeutic benefits. The chewing gum Dikamali is one of the key medications in the Indian medical system [26].Rats were subjected to paracetamol-induced liver injury, and the hepatoprotective and antioxidant activities of Gardenia gummifera's whole plant methanolic extract (GGME) was examined. Moreover, the GGME separated toluene, ethanol, 2-butanone, n-butanol, and petroleum ether based on the polarity of the solvents.In paracetamol-induced liver damage, the dramatically increased blood enzymatic levels of Aspartate Aminotransferase (AST), Alanine Transaminase (ALT), Alkaline Phosphate (ALP), and total Bilirubin were significantly recovered towards normality by the GGME in a dose-dependent manner. Histopathological analysis of liver section significant protection against paracetamol-induced hepatotoxicity was added to the biochemical observations.When the inquiry was furthered using GGME fractions, the highly raised serum levels of the enzymes AST, ALT, ALP, and total bilirubin (TB) were greatly reduced and returned to normal. The liver weight of rats with paracetamol-induced liver damage and pentobarbitone-induced sleeping time revealed significant values with nbutanol fraction, respectively.DPPH scavenging assays, which were also evaluated for in vitro antioxidant activity, were shown to be considerably positive in a dose-dependent manner. The findings of this work strongly suggest that paracetamol-induced liver damage in experimental mice can be prevented by GGME and n-butanol fraction, which exhibit powerful hepatoprotective effect [27].

EUPHORBIA TIRUCALLI L.

Relating to the Euphorbiaceae family is Euphorbia tirucalli Linn. It is a native to temperate regions and is a blooming shrub or small tree. Its common name, pencil tree, comes from the fact that its twigs resemble pencils [28]. E. tirucalli is widely planted as a hedge plant in gardens and along cultivated fields in the drier parts of India [29].The common name for E. tirucalli is Aveloz. It is a native of Africa and America, but it has successfully acclimated and spread far over India, especially in the drier regions of Bengal and South India, where it has essentially grown up in hedge. It was created in Berar to provide young mango trees with protection from direct sunshine [30–32].Rats' liver damage caused by CCl4 was tested using an aqueous extract of E. tirucalli. The extract significantly reduced serum bilirubin, cholesterol, triglycerides, and tissue lipid peroxidation levels, resulting in significant hepatoprotective action. The tissue's GSH level rose [33].

RHUS OXYACANTHA

Two species of the genus Rhus are known in Tunisia: [Rhus oxyacantha (Shousb). Cav = R. oxyacanthoides for example Rhus tripartita (Ucria) Grande, Dum. cours Rhus pentaphylla and [=R. tripartitum (Ucria) D.C. =Searsiatripartita (Ucria) Moffet]. [34] The Tunisian plant Rhus oxyacantha, also referred to as "Jdéri," is used in traditional medicine to treat digestive disorders. [35,36] Rhus oxyacantha is a plant that grows widely throughout North Africa, particularly in the steppes of the desert and other arid and semi-arid regions. It is not only found in Tunisia. [37,38] It also exists in the steppes of Sicily and Western Asia, and many nations located in the aforementioned regions employ it in folklore and traditional medicine. [37,39,40] Several portions of the Rhus oxyacantha plant have long been utilised in traditional Arabian medicine to treat digestive and circulatory diseases as well as inflammatory conditions. [41] The total phenolic, flavonoid, and condensed tannin levels of the RE were high. The extract's considerable and powerful free radical scavenging activity was demonstrated by in vitro antioxidant systems. The R. oxyacantha active extract's HPLC fingerprint revealed the presence of five phenolic compounds, with higher concentrations of catechol and gallic acid. According to the in vivo findings, DDT increased the levels of liver markers (ALT, AST, and LDH) in the serum of experimental animals after a single intraperitoneal injection. As a result, there were higher levels of lipid peroxidation, a

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significant induction of SOD and GPx, metallothioneins (MTs), and a concurrent decrease in non-protein thiols (NPSH) in the liver. It also increased the oxidative stress markers, which led to higher levels of lipid peroxidation. On the other hand, pre-treating rats with RE at doses of 150 and 300 mg/kg body weight significantly decreased serum transaminases and LDH in treated rats. By using a plant extract to combat DDT, it was found that the levels of hepatic MTs, antioxidant enzyme activities, and thiobarbituric reactive chemicals all significantly decreased. These biochemical alterations were in line with histological findings and suggested a significant hepatoprotective effect of RE at both dosages. These findings support the traditional use of this plant by strongly indicating that treatment with ethyl acetate extract normalises several biochemical markers and shields the liver against DDT-induced oxidative damage in rats. The examination of the traditional claim on this plant is aided by the fact that the extract normalises a number of biochemical indicators and safeguards the liver against DDT-induced oxidative damage in rats. [42]

CERIOPS DECANDRA (GRIFF.)

A member of the Rhizophoraceae family, Ceriopsdecandra (Griff) Ding Hou is a mangrove plant. The bark and leaf of C. decandra are used as remedies for hepatitis and ulcers in folk medicine [43].

The leaf, bark, collar, flower, and hypocotyls of C. decandra have hepatoprotective properties. In vitro antioxidant studies using the DPPH, HRSA, NO, FRAP, and LPO assays were performed. The leaf extract, which was found to be the most potent, was used to test the in vivo hepatoprotective efficacy and the LD50.The following was done to test the in vivo hepatoprotective activity: Group 1: Control animals; Group 2: Animals treated with carbon tetrachloride (CCl4); Group 3: Animals treated with silymarin (100 mg kg-1 bwp.o.); Groups 4–6: Animals treated with C. decandra (100, 200, and 400 mg kg-1 bw), respectively. Standard procedures were used to compute the histopathological scores. Leaf extract demonstrated the highest levels of antioxidant scavenging abilities among the several plant parts that were chosen. Extract from C. decandra was found to be non-toxic up to 2000 mg kg1 bw in a study on the oral acute toxicity. When compared to hepatotoxin groups, the levels of SGOT, SGPT, ALP, bilirubin, CHL, and LDH were found to be considerably lower (p 0.05), indicating that the leaf extract's in vivo hepatoprotective nature is dosage dependent. Histopathological results comparing control and high dose (400 mg kg1 bw) of leaf extract-treated mice did not reveal any appreciable differences. The leaf extract underwent a preliminary phytochemical study, which identified phenolic groups, alkaloids, triterpenoids, flavonoids, catechin, and anthraquinone. In conclusion, the presence of distinct secondary metabolites and their antioxidant scavenging abilities may be the cause of the hepatoprotective properties of the C. decandra leaf extract [44].

POLYGONUM ORIENTALE

Chinese herbal pharmacopoeias list Polygonum orientale L. (Family: Polygonaceae) as a food and medicine [45]. Several natural materials have therapeutic qualities; flavonoids are among the best-known examples of potent plant-based pharmacological substances.Many flavonoids, including taxifolin and quercetin, have been identified in this plant through phytochemical research. Furthermore, phenolics such gallic acid and protocatechuic acid were discovered [46]. China has employed the entire plant to treat a number of ailments including arthritis, edoema, diarrhoea, fractures, urticarial, and muscular injuries [47].

The ethanolic extract of P. orientale (POE) fruits has hepatoprotective properties against acute liver damage brought on by carbon tetrachloride (CCl4) (ALI). For five days straight, mice were pre-treated with POE (0.1, 0.5, and 1.0 g/kg) or silymarin (0.2 g/kg), and on the fifth day, ALI was induced by giving the mice a dosage of 0.175% CCl4 (ip). Analyzing cytokines and anti-oxidative activity in blood and liver samples.High-performance liquid chromatography was used to determine the bioactive POE components (HPLC). According to tests for acute toxicity, POE's mouse LD50 was higher than 10 g/kg. Animals pre-treated with POE (0.5, 1.0 g/kg) had significantly lower levels of the enzymes alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) in their serum, as well as less severe liver lesions overall.The levels of tumour necrosis factor-a (TNF-a), malondialdehyde (MDA), nitric oxide (NO), interleukin-1b (IL-1b), and interleukin-6 (IL-6) were all decreased by POE, and superoxide dismutase (SOD), glutathione peroxidase (GPx), and glutathione reductase (GRd) activities were all enhanced.Protocatechuic acid, taxifolin, and quercetin all showed peaks on the

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HPLC at 11.28, 19.55, and 39.40 min, respectively. In conclusion, the hepatoprotective activity of POE against CCl4-induced ALI was reportedly linked to its anti-inflammatory and antioxidant properties [48].

MACROTHELYPTERIS TORRESIANA

A species of fern known as Macrothelypteristorresiana (Gaudich), also known as Lastreatorresiana Moore and belonging to the Thelypteridaceae family, is indigenous to tropical and subtropical regions of the world. The fern is strong and has a small, creeping rhizome [59,50].The leaves and roots of M. torresiana have a variety of reputed medicinal uses in conventional medicine. The tribes of Pakistan, India, and China use the aerial portions to treat fever, pain, granulation, healing, and odour reduction in chronic skin ulcer and inflammation. Moreover, it is employed in Chinese folk medicine to relieve edoema in patients with kidney issues [51, 52].

High performance thin layer chromatography is used to identify the polyphenolic compounds present in the ethanol extract from M. torresiana aerial parts (EEMTAP), which has the potential to protect the liver (HPTLC). In Wistar albino rats, the hepatoprotective activity of EEMTAP was examined at dosages of 300 and 600 mg/kg, per os (p.o.).Different biochemical parameters like serum glutamate-pyruvate transaminase (SGPT), alkaline phosphatase (ALP), and serum glutamic oxaloacetic transaminase (SGOT) that were elevated by carbon tetrachloride (CCl4) intoxication showed a significant decrease in activities in the extract and silymarin treated animal groups. By using EEMTAP and silymarin, the levels of total bilirubin, total protein, and liver weight were also brought back to normal.After CCl4 administration, glutathione (GSH) and catalase (CAT) levels in the liver dropped, whereas hepatic lipid peroxidation (LPO) levels increased. By using EEMTAP and silymarin, the levels of these hepatic antioxidant enzymes were likewise restored to normal.The biochemical results were corroborated by histological examinations, and EEMTAP therapy at doses of 300 and 600 mg/kg, p.o. was successful in reversing CCl4-induced hepatotoxicity in rats.A straightforward HPTLC examination was performed to identify the polyphenolic compounds present in EEMTAP, and the results showed that caffeic acid, a phenolic acid, and quercetin, a flavonoid, were both present. The suggested HPTLC method is clear and easy to follow, and it effectively separates quercetin and caffeic acid from other EEMTAP ingredients [53].

AQUILARIA AGALLOCHA

The thymelaeacea family member Aquilaria agallocha is referred to as Agarwood in English, Agar in Hindi, and Aguru in Sanskrit [54]. For thousands of years, agarwood has been used for a variety of purposes around the world. Susruta Samhita and Shahih Muslim, as well as other traditional East Asian medicinal systems, have all acknowledged using it [55,56].Susruta Samhita and Shahih Muslim, as well as other traditional East Asian medicinal systems, have all acknowledged using it [55,56]. Aphrodisiac, anodyne, acrid, astringent, aromatic, cardiac tonic, bitter, carminative, fragrant, and stimulant are some of the therapeutic qualities traditionally used to describe the bark, root, and leaves of the heartwood of agarwood.Agarwood is also used as a mouth freshener, carminative, and appetiser as well as a treatment for acute discomfort including headaches and colic during pregnancy [57].

Animals in Group I received 1% CMC treatment for 8 days. Animals in Groups II, III, IV, and V were first given treatment with "1% CMC." For seven days, take 1 ml/kg/day, AAE 200 mg/day, AAE 400 mg/day, and silymarin 100 mg/kg/day, respectively. On the eighth day, take PCM 3 g/kg b. wt. in a single dose. The animals were slaughtered and the blood was drawn through the retro-orbital plexus under low sedation 24 hours after the previous dose by PCM. Several biochemical markers, including ALT, AST, ALP, LDH, bilirubin, cholesterol, TP, and ALB, were used to evaluate the hepatoprotective potential. When compared to group II rats, group IV rats demonstrated a significant (p 0.01) decrease in ALT, AST, ALP, LDH, cholesterol, bilirubin, liver weight, and relative liver weight while exhibiting a significant (p 0.01) increase in final b. wt., TP, and ALB levels. AAE's 400 mg/kg/day hepatoprotective potential was on par with silymarin's usual dose of 100 mg/kg/day. The histopathological findings provided strong support for the study's conclusions. Comparing to the normative group [58].

II. CONCLUSION

Hepatic disease continues to be a global health problem despite tremendous breakthroughs in current medicine, therefore the search for novel drugs is still underway. In Chinese ethnoclinicalpractise and Western medicine, a

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variety of plant-based preparations are utilised to treat liver problems. Several of these medications work as radical scavengers, while others are mutagens or enzyme inhibitors. The presence of flavonoids, alkaloids, terpenoids, glycosides, and steroids in the plants may be the cause of their hepatoprotective effects. Capsules containing energetic extracts, fractions, or combinations of fractions and extracts from flowers may also be quite effective. To treat severe liver diseases brought on by harmful chemicals, viruses (such as Hepatitis B and C), excessive alcohol use, and repeated administration of medications like paracetamol, rifampicin, and isoniazid, plant extracts (combos or individual drugs) must be effective enough. It is impossible for a single medication to be effective against all forms of severe liver diseases. The utilisation of local medicinal plants should be advanced in formulations, together with appropriate pharmacological research and clinical studies. Standards of protection and efficacy must be used to regulate the production of plant products.

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