Global uses of traditional herbs for hepatic diseases and other pharmacological actions: A comprehensive review

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Abstract

Hepatocellular carcinoma (HCC) is the 7th most common cancer and the 3rd leading cause of cancer-related death worldwide. It is resistant to the majority of chemotherapeutics and has a dismal prognosis. Hepatocellular carcinoma is a prevalent complication of chronic liver disease (CLD) in India. Primary liver cancer is the 6th most common cancer worldwide and the 4th most prevalent cause of cancer-related death. In 2018, it affected 841,000 people and caused 782,000 deaths around the world. Thus, research into the tumor cycle and its prevention through suitable herbal (Unani/Ayurvedic) medication is critical for reducing the impact of primary liver cancer. Treatment options for end-stage liver cancer are limited, necessitating costly liver transplantation, which is unavailable in most countries. Here, we present the results of a comprehensive literature survey to determine the benefits of using various herbs with liver protective and antioxidant properties. This information will be useful to researchers working on liver carcinoma and free radical scavenging, both of which are important in curbing potential carcinogens.

Key words: HCC, anti-oxidant, *Bauhinia variegata*, *Picrorhiza kurroa*, traditional Unani medicine

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Introduction

Hepatocellular carcinoma (HCC) is one of the most common types of solid tumor. Currently, more than 800,000 HCC cases are diagnosed annually around the world.[1] This tumor is highly aggressive, as currently evidenced by the annual mortality rate of approx. 700,000 worldwide.[2] Primary liver cancer is the 3rd leading cause of cancer-related death and the 7th most prevalent cancer worldwide. About 782,000 people died as a result of it in 2018, and it affected 841,000 people around the world. Malignant hepatocytes are the origin of the cancer known as HCC.[3,4] Currently, only a few therapeutic alternatives are available for HCC patients. Thus, the first step in developing new therapeutic techniques entails gaining a thorough understanding of the biochemical underpinnings of HCC.[5] Pathological mechanisms that lead to various chronic liver disorders include the progressive destruction and regeneration of liver parenchyma. Some of the most prevalent chronic liver illnesses are viral hepatitis, alcoholic or nonalcoholic fatty liver disease, autoimmune hepatitis, cirrhosis, and HCC.[6] Their main causes are excessive alcohol use, viral infection, obesity, diabetes, and drug-induced liver injury. Chronic liver illnesses cause approx. 3.9–6.9 deaths per 100,000 people in various parts of the world.[7] Hepatocellular carcinoma is an especially prevalent complication of chronic liver disease (CLD) in India, with over 22,000 new cases of primary liver cancer recorded annually. Secondary liver cancer is 20 times more common than primary liver cancer.

When compared to other cancers, HCC is extremely complex. It is most commonly linked to chronic liver illnesses like hepatitis or cirrhosis, which can be caused by a variety of factors. Cirrhosis is a precursor to most HCC cases, while developing HCC deteriorates liver function; thereby, HCC and cirrhosis both are impacting each other. Furthermore, HCC is resistant to a wide range of toxins as well as the majority of chemotherapeutics. Several clinical trials have used high dosages of chemotherapeutic drugs to overcome the resistance of HCC. However, such efforts have failed to provide any significant benefits for HCC patients. Another distinguishing feature of HCC is the inherent tendency of HCC cells to penetrate the portal vein and develop in its lumen; the HCC cells might then be transported away via the bloodstream, thereby resulting in distant metastasis.

Hepatocellular cancer therapy choices are severely limited due to such difficulties. Surgical resection, ablation and chemoembolization are effective only in a small number of individuals. Protein kinase inhibitors, such as sorafenib, improve survival for a limited period. Hepatocellular carcinoma has an exceptionally low overall survival rate of 4%, underscoring therapeutic limitations and posing a serious health burden. For individuals with cirrhosis and end-stage liver disorders, liver transplantation is currently the only curative option.[8]

The Unani system of medicine is one of the oldest traditional medical systems, with centuries of experience in treating CLD and cirrhosis. A wide range of single and compound medication formulations have been shown to help people with CLD. Antifibrotic and liver regeneration properties are the most common uses for these formulations.[9]

Antioxidants

In recent years, numerous studies have emerged regarding the potential role of nutrition in illness prevention. Antioxidants, particularly those produced from natural sources (e.g., herbal medications), such as Indian medicinal plants, are particularly important in this context. Consequently, antioxidants have numerous potential applications, especially in human health, such as illness prevention and treatment.[10,11] Radiation exposure, environmental contaminants and metabolized medication by-products all produce free radicals. Antioxidants are compounds that prevent oxidation. They are also known as "powerful antioxidants" since they use radicals to produce minor reactive species. Exogenous and endogenous antioxidants are divided in 2 categories based on their source. Antioxidants help to prevent diseases such as cancer, diabetes, inflammation (e.g., liver inflammation, i.e. cirrhosis, CLD, cardiovascular disease (CVD), cataract, nephrotoxicity, and neurological diseases.[12]

Hepatocellular carcinoma

Hepatocellular carcinoma is a rapidly growing clinical concern that mostly affects people with cirrhosis and CLD. It is most common in Africa and Asia, where the endemic frequency of hepatitis C virus (HCV) and hepatitis B virus (HBV) greatly promotes the development of CLD and, as a result, HCC. Hepatocellular carcinoma is generally identified at an advanced stage after observing weight loss, indications of decompensated liver disease, and right-upper-quadrant pain; however, it can now be detected at an earlier stage through cirrhosis screening, serum alpha-fetoprotein (AFP) measurements and cross-sectional imaging tests. Understanding and characterizing hepatic cancer stem cells (HCSs) is crucial for understanding HCC origins.[13] If the nature of HCSs can be thoroughly defined, patients with end-stage liver disease will receive effective and well-organized care more often.[14] Organ shortages remain a key limiting factor even in developed countries, with only a small percentage of all patients having access to transplantation. Local ablative therapy, such as chemoembolization, potentially innovative chemotherapeutic drugs and radiofrequency ablation (RFA), may bring relief to and prolong the life of these patients. With the introduction of very effective direct-acting

antivirals (DAAs) for hepatitis,[15] the incidence of hepatitis-related HCC is prognosed to decrease.[16] The progression and management of HCC will most likely be determined by a mix of virus-specific, environmental, immune-related, and host genetic factors.[18]

Pharmacological applications of Unani herbs

Kachnar (*Bauhinia variegata* Linn.)

Bauhinia variegata L. is a medium-sized ornamental plant that grows up to 10–15 m tall and belongs to the Fabaceae family and Caesalpinioideae subfamily. Its common name in English is mountain ebony, while Kachnar is its Urdu name. It is a deciduous tree that loses its leaves in November and December, and remains leafless between January and April. When trees are young, they have a smooth, dark brownish bark with grey puberulent branches. The species is native to Asia (specifically India, Pakistan, China, and Nepal) (Fig. 1 and Table 1).

Hepatoprotective activity

The hepatoprotective activity of Kachnar in Sprague Dawley rats examined utilizing oral doses of 100 mg/kg and 200 mg/kg stem bark extracts exhibited hepatotoxic action against carbon tetrachloride-induced hepatotoxicity. These extracts specifically increase total protein levels and decrease the levels of alanine transaminase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), and total lipids.[18] Leaf infusions are used to treat piles, worms, tumors, diarrhea and dysentery, and also exhibit laxative properties.[19]

Manoj et al. reported that ethanolic extracts of *Bauhinia variegata* protect rats against carbon tetrachloride-induced liver damage. A solution of carbon tetrachloride (1 mL/kg) diluted in olive oil (1:1) was administered orally to cause liver injury. The standard medicine was silymarin (100 mg/kg). The potencies of *Bauhinia variegata* ethanolic extract (BVEE) at 400 mg/kg and 600 mg/kg were higher compared to BVEE at 200 mg/kg and 100 mg/kg.[20]

Yadava and Reddy reported that the trypsin inhibitory activity of *Bauhinia variegata* anti-inflammatory activity was due to flavanone glycoside, which is found in the roots.[21]

Anti-tumor activity

Azevedo et al. investigated Kachnar anti-tumor activity because an insulin-like protein was detected in its leaves, and since it has also been widely utilized as an anti-diabetic treatment.[22] Anti-tumor potential of Kachnar was investigated and it was discovered that an ethanolic and aqueous extract of its stem had an anti-tumor impact on Swiss albino mice with Dalton's ascetic lymphoma (DAL).[23] Experiments on induced DEN liver tumors and human cancer lines showed chemopreventive and cytotoxic effects.[24]

Antioxidant activity

The antioxidant activity of Kachnar, which contains a potent flavonoid called quercetin, influences several enzymatic activities via interactions between biomolecules and quercetin's chemical component.[25] An antioxidant activity evaluation of aqueous and ethanolic extracts of Kachnar root was performed in vitro by scavenging free radicals with 1,2-diphenyl-1-2 picrylhydrazyl (DPPH).[26] The antioxidant and DNA-protecting activities of a methanolic extract of Kachnar bark MEB (methanol extract *Bauhinia variegata*) were observed in vitro against H_2O_2-induced oxidative damage to pBR322 plasmid DNA. The MEB and its polar sub-fractions EAB (ethyl acetate fraction *Bauhinia variegata*), NBB (n-butanol *Bauhinia variegata*) and REB (remaining extract *Bauhinia variegata*) showed high antioxidant activity and are reported to have the potential to prevent H_2O_2-induced oxidative damage to pBR322 DNA. The phenolic/flavonoid chemical richness of Kachnar bark extract/fractions may account for their H_2O_2 high antioxidant activity and DNA protective capabilities.[27]

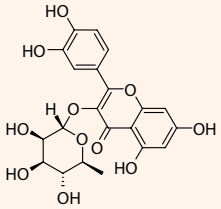
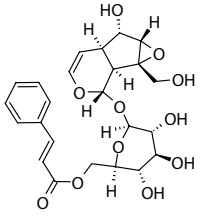
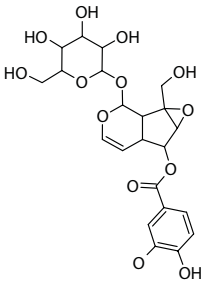
Active constituents

Kaempferol -3-glucoside, β-sitosterol, lupeol, tannins,carbohydrates,crude protein, fibers, calcium, amides,reducing sugars, vitamin C, quercitrin, apigenin, phosphorus, quercetin, rutin, apigenin -7-O-glucoside, dotetracont-15-en-9-ol and heptatriacontan-12,13-dioletc.

Botanical name: *Bauhenia Veriagata* Linn.
Family: Leguminosae Caesalpinioideae

Fig. 1. Kachnar and its active constituent

Table 1. Summary of Unani drugs

Name of the plant	Common names	Details about the plant	Active constituents	Structure	Uses	References
Kachnar (*Bauhinia veriagata* Linn), (Leguminosae Caesalpinioideae)	mountain ebony (English), Rakta kanchan (Marathi), Kachnar (Hindi) Kempu mandara (Kannada), Shemmandarai (Tamil), Daevakan-chanamu (Telgu)	It may be found all across India, particularly in Punjab and central and south India, up to an altitude of 1300 m in the sub-Himalayan and outer Himalyan regions	kaempferol-3-glucoside, β-Sitosterol, lupeol, tannins, carbohydrates, crude protein, fibers, calcium, amides, reducing sugars, vitamin C, quercitrin, apigenin, phosphorus, quercetin, rutin, apigenin-7-O-glucoside, dotetracont-15-en-9-ol and heptatriacontan-12, 13-diol etc.	 quercetin	bronchitis, leprosy, inflammation, bacterial infection, liver diseases, diarrhea, dysentery, skin illnesses, leprosy, intestinal worms, wounds, ulcers, fungal infection, ulcers, and tumors	19–26, 32–35
Kutki (*Picrorhiza kurroa*) (Plantaginaceae)	Kardi, Karoi, Karwi (Hindi), Kutki (Urdu), Kurki (Nepali), Katukhurohani (Malayam), Anjani (Arishta, Katumbhara (Sanskrit), Katuka-rogani, Katukarogani, Katukkurohini (Telugu), Acokarokini, Akutam, Amakkini (Tamil)	It is found primarily in the Himalayan regions, which includes from Garhwal to Bhutan, north Burma, west China, and southeast Tibet. The species can be found in huge numbers at elevations of 3000–5000 m.	Picroside I, picroside II, and cucurbitacins, iridoid glycoside d-mannitol, kutkiol, kutki sterol, and apocynin. This species has only been assessed for a few biological functions, including antimicrobial, antidiabetic, anti-asthmatic, hepatoprotective, antioxidant, immunomodulatory, anticancer, anti-inflammatory, nephroprotective, analgesic, and cardioprotective.	 picroside I  picroside II	anemia, stomach ache, asthma, obesity, malaria, fever, skin illnesses, bronchial asthma, immunological disorders, and viral hepatitis	44–46, 50–54

Antimicrobial activity

Parekh et al. discovered that Kachnar has antimicrobial properties and is effective against Gram-negative bacteria, which were suppressed using Kachnar leaf extract. However, the antibacterial range of Kachnar is somewhat limited. The polar extracts were effective against *Escherichia coli*, *Pseudomonas* spp. and *Klebsiella pneumoniae*. The antibacterial, bio-enhancement and anti-inflammatory capabilities of *Staphylococcus aureus* are inhibited by the Kachnar bark powder.[28]

The antibacterial activities of methanolic Kachnar flower extracts were assessed by studying Gram-positive *Staphylococcus epidermis*, *Bacillus subtilus* and *S. aureus*, and Gram-negative *E. coli*, *S. flexineria* and *P. aeruginosa*. Microorganism development was suppressed depending on specific dosages of these methanolic extracts.[29]

Antiulcer activity

Kachnar's antiulcer activities were reported in rats, and an ethanolic extract of Kachnar stems showed an antiulcer efficacy against stomach ulcers caused by pyloric ligation and aspirin-induced ulcers. The volume of gastric acid secretion was also reduced by the ethanolic extract from stem of Kachnar and the total acidity, free acidity and ulcer index control became lower as the ulcer healed.[30,31]

Arain et al. reported that pain, diabetes, infections, ulcers, jaundice, and leprosy can all be treated using Kachnar stems, roots and leaves.[32]

Antibacterial activity

When Kachnar extracts were used against *S. aureus*, *Bacillus cereus*, *Pseudonomas pseudoalcaligenes*, *K. pneumoniae*, and *E. coli*, they exhibited antibacterial activity againt all these species. Specifically, methanolic extracts have a higher antibacterial activity than aqueous extracts.[33]

In another study, it has been reported that when the cup plate method was used, Kachnar demonstrated antibacterial and antifungal activities in 50 mg/mL, 100 mg/mL and 200 mg/mL petroleum ether, chloroform, acetone-water, and water extracts. Gram-positive bacteria, *S. aureus* and *E. coli*, were used to test the antibacterial activity, while *Candida albicans* and *Aspergillus niger* were utilized to test antifungal activity. Kachnar displayed an intensive antibacterial and antifungal action.[34]

Anti-inflammatory activity

Mohamed et al. identified anti-inflammatory and analgesic activities of Kachnar, and reported that leaves of Kachnar contain novel triterpene saponins that reduce edema, while also lowering PGE2 (prostaglandin E2) levels in serum, liver homogenate and granuloma. Triterpene saponin treatment reduced the diameters of hepatic and pulmonary granulomas, which is thought to be related to its anti-inflammatory properties. Furthermore, in both visceral and cerebral nociceptive mice models, the chemical constituents present in the Kachnar showed analgesic effects.[35]

In another investigation, it was shown that Kachnar reduced the anti-inflammatory actions of several flavanol glycosides found in *Bauhinia* spp. Flower buds can be used to treat cough, piles, liver disorders, and eye problems, as well as act as an astringent in hematuria and catamenia.[36]

A study of the anti-inflammatory properties of mountain ebony found that extracts contain a sufficient amount of anti-inflammatory properties.[37] Gunalan et al. reported strong anti-inflammatory actions, as determined with gas chromatography–mass spectrometry (GC-MS) analysis.[38]

Antidiabetic activity

Azevedo et al. reported that leaf and stem bark of Kachnar contain insulin-like proteins, which are widely employed as an anti-diabetic ingredient in a variety of popular treatments.[22]

Dewangan et al. reported the discovery of D-pinitol, a bioactive chemical, in Kachnar leaves. This substance is a natural product of the cyclic polyol group and has hypoglycemic properties.[39] Shahana et al. reported antidiabetic activities of Kachnar since this plant contains a domain structure with the same amino acid sequence as insulin. In a strepto-zotocin-induced diabetes model, they found that insulin can successfully lower blood glucose levels in hyperglycemia. The high blood glucose levels in streptozotocin-induced and alloxan-induced diabetic rats were lowered when alcoholic and hydroalcoholic extracts of Kachnar leaves were administered orally at a dosage of 200 mg/kg.[40]

Wound-healing activity

A study by Gyawali et al. showed that Kachnar in combination of other plants has satisfactory wound healing properties compared to standard drugs. Kachnar, *Rhododendron arboreum* and *Myrica esculenta* can be combined in various ratios to create a polyherbal liniment. They investigated antioxidant and wound-healing properties of polyherbal ointments containing methanolic extracts of Kachnar, *Myrica esculenta*, *Rhododendron arboretum*, and *Rhododendron esculenta*. The DPPH assay was used to examine the antioxidant activities of Kachnar, *Myrica esculenta*, *Rhododendron arboreum*, *Pyrus pashia*, and *Psidium guajava*. They combined Kachnar, *Rhododendron arboreum* and *Myrica esculenta* in a 1:1:2 ratio to prepare a 10% w/w ointment. In the excision wound model, the herbal ointment-treated rats were completely healed, but the framycetin-treated, blank and control groups still had 2.72%, 4.5% and 5.73% wound areas, respectively.[41]

In another study, Sharma et al. evaluated the wound-healing activity of Kachnar using the percentage of wound closure, time of epithelialization, hydroxyproline estimation, and histological examinations of the granulation tissue for the excision wound model, and tensile strength measurement for the incision wound model. Both aqueous and ethanolic extracts of the root of *Bauhinia variegata* Linn. demonstrated considerable wound healing efficacy. In both wound types, ethanolic extract demonstrated wound healing activity comparable to the control. The histological assessment confirmed the outcome of wound healing activity. The phenolic content of ethanolic and aqueous extracts was determined to be 14.88 g/mg of pyrocatechol equivalents and 22.62 g/mg of pyrocatechol equivalents, respectively. The high level of flavonoids in the ethanolic and aqueous extracts resulted in substantial wound healing activity.[42]

Kutki (*Picrorhiza kurroa* Royle ex Benth.)

"Picros" means bitter in Greek, whereas "rhiza" denotes root. *Picrorrhiza kurroa* is thus referred to as bitter root. In Ayurveda and Unani medicine, a plant genus in the Plantaginaceae family is known as "Kutki", "Kurro" or "Indian gentian". Due to potent iridoid glycosides present in the plant, a large body of pharmacological research has demonstrated its anti-cancer activity. The medication Kutki is made up of dried rhizome and root of *Picrorhiza kurroa*. It is a low-growing perennial herb, more or less hairy, that grows up to 20 cm tall. *Picrorhiza kurroa* is among India's best-known medications, widely used from Sikkim to Kashmir in the northwestern Himalayas (Fig. 2, Table 1).

Antidiabetic activity

Picrorhiza kurroa inhibits hypoglycemic activity and the major phytoconstituents present in these plants show potent antidiabetic activity.[43,44] He et al. reported that in rats with alloxan-induced diabetes, *Picrorhiza kurroa* plant extracts lowered blood glucose levels. Streptozotocin-induced diabetic rats were administered a herbal formulation that reduced the expression of malondialdehyde (MDA) and nicotinamide adenine dinucleotide phosphate (NADPH)-oxidase-dependent superoxide production in the diabetic kidney, demonstrating that *Picrorhiza kurroa* affects diabetic nephropathy by inhibiting redox active inflammation.[45] Husain et al. investigated the significant antidiabetic potential of this plant's alcoholic extract in type 2 diabetes mellitus caused by streptozotocin-nicotinamide in rats and obtained similar results.[46]

Active constituents

Glycosides,1-(4-hydroxy-3-methoxyphenyl)ethanone, 1-(4-hydroxy-3-methoxyphenyl)ethanone, 3-phenylprop-2-enoicacid, veronicoside

Botanical name: *Picrorhiza kurroa*
Family: Plantaginaceae

Fig. 2. Kutki and its active constituent

In another study, Husain et al. investigated the mechanism of antidiabetic effects in diabetic (streptozotocin-induced) experimental mice, in which *Picrorhiza kurroa* extracts boosted insulin-mediated GLUT-4 expression, thereby increasing glucose absorption by skeletal muscles.[47]

Husain et al. in yet another study examined *Picrorhiza kurroa* for its potential role in cell induction in insulin production, with the hypothesis that it improved cell regeneration and thereby provided relief from type 1 diabetes.[47]

Hepatoprotective activity

Hepatocytes are cells that make up the major parenchymal tissue in the liver. Roughly 70–85% of the liver's mass consists of fat. Hepatic damage is caused by the death of hepatocytes when the levels of normal serum transaminase enzymes are elevated.[48] Jia et al. reported that by enhancing intestinal absorption, the herbal extract provided advanced nutraceutical activity for superior hepatoprotection.[49]

The ethanol resistance of picroliv isolated from *Picrorhiza kurroa* has been noted in toxicity investigations in comparison to typical hepatoprotective drugs, such as Catapol, silymarin and andrographolide. The animal model exhibited good response to these medications. The ALP levels have dropped, while enzymatic assays such as glutamic-oxaloacetic transaminase (GOT), ALT and aldehyde have shown greater inhibitions compared with ALP. Therefore, it was suggested that *Picrorhiza kurroa* causes potent hepatoprotective effect.[50]

Hepatoprotective efficacy of pirocliv against ethanol-induced toxicity in rats is dosage-dependent.[51] In rats, ethanolic extract of *Picrorhiza kurroa* rhizomes and roots showed hepatoprotective activity against rifampicin- and isoniazid-induced hepatitis. The plant minimized drug-induced changes.[52,53] Floersheim et al. reported that in mice poisoned with lethal quantities of Amanita mushrooms, the therapeutic efficiency of Kutki was higher than that of normal silybinin.[54]

Anticancer activity

The anticancer properties of *Picrorhiza kurroa* are due to its constituents, such as picroside I, picroside II , cucurbitacins, apocynin, and others.[55] Mallick et al. discovered anticancer activity of *Picrorhiza kurroa* and reported that a failure of the apoptosis system could result in endless cell division and proliferation. The dichloromethane fraction of *Picrorhiza kurroa* demonstrated effective anticancer activity and may be worth investigating for cancer therapy.[56] Picroliv inhibited chemically caused cancer in rats in a dosage-dependent manner, thereby increasing the survival rate to roughly 65%,[57] while N-nitrosodiethylamine-induced hepatocarcinogenesis was greatly reduced by *Picrorhiza kurroa* extract.[58]

Antioxidant activity

Kalaivani and Mathew found that antioxidant agents present in this plant act as radical scavengers, thereby protecting the human body from a variety of ailments. Activity of liver enzymes was lower in patients with liver cirrhosis after therapy with *Picrorrhiza kurroa plant* extract.[59] Deshpande et al. showed that liver enzyme activity was lowered in liver cirrhosis patients after therapy with the *Picrorhiza kurroa* plant extract.[60] Such extracts have been shown to be efficient antioxidants for evaluating lipid peroxidation inhibition; it was demonstrated by Rajkumar et al. who used radical scavenging tests, ferric reducing antioxidant property assay and thiobarbituric acid assays.[61]

Picrorrhiza kurroa rhizome ethanol extract at 20 mg/kg b.w. healed the stomach wall of indomethacin-induced gastric ulcerated rats through an in vivo free radical scavenging action. Krupashree et al. used a variety of antioxidant testing methods to confirm the antioxidant efficacy of *Picrorrhiza kurroa* leaf fractions. The extract shown considerable reducing capability along with antioxidant properties, with IC50 values of 75.16 3.2 g/mL for DPPH radical scavenging and 55.5 4.8 g/mL for metal chelating, respectively. The *Picrorrhiza kurroa* extract's antioxidant and radical scavenging properties suggest

that it may be useful as a food supplement and source of natural antioxidants for a variety of oxidative stress-related disorders.[62]

Anti-inflammatory activity

Picrorrhiza kurroa rhizome is a traditional medicine used to treat inflammatory conditions.[63] The active phytoconstituent apocynin, found in root extracts, has been shown to have anti-inflammatory activities. The fact that *Picrorrhiza kurroa* inhibits edema at a rate of 29.8% indicates that it is an effective anti-inflammatory medication.[64]

The rhizome extract of *Picrorrhiza kurroa* considerably reduces joint inflammation. It also has anti-inflammatory properties against chemically generated inflammation and might be considered a high-quality natural analgesic.[65]

The anti-inflammatory effects and production of thromboxane A2 was suppressed by apocynin in a dosage-dependent manner, but the release of prostaglandins E2 and F2α increased. Arachidonic acid-induced aggregation of bovine platelets was reduced by apocynin, potentially by the reduction of thromboxane production.

Immunomodulatory activity

The immunomodulatory activity of *Picrorrhiza kurroa* was investigated, as well as the immunostimulatory activity of biopolymeric fractions. Biopolymeric fractions have been isolated from medicinal plants and used as a source of therapeutic agents. The most promising biopharmacological activities of these biopolymers are their immunomodulatory effects. The biopolymeric fraction RLJ-NE-205 was isolated and purified from the rhizomes of *Picrorhiza kurroa*. An immunomodulatory agent is a type of medicine that, depending on its effect on the immune system, can either stimulate or suppress the immune system.[66] In mice, ethanolic extract of *Picrorrhiza kurroa* leaves was able to stimulate humoral and cell-mediated immune system components, as well as phagocytosis.[67]

In another study, Hussain et al. reported that antigen non-specific defense was aided by 2 potent anticomplementary polymeric fractions. Those findings support the hypothesis that preparations from *Picrorrhiza kurroa* roots may have an impact on immunological processes, as the alcoholic extract of the root is more effective than the aqueous extract in causing a delayed hypersensitivity reaction. In mice, the effects of an ethanolic extract of each medication on delayed hypersensitivity, humoral responses to sheep red blood cells, skin allograft rejection, and reticuloendothelial system phagocytic activity were investigated. *Picrorhiza kurroa* has been found to be an immunostimulant with both cell mediated and humoral actions.[68]

Cardioprotective activity

Nandave et al. reported that rats given 200 mg/kg *Picrorhiza kurroa* root extract alone showed no significant alterations; however, no changes were observed in a pre-processed in vivo model when given isoproterenol, which induced hemodynamic and left ventricular dysfunction, lipid peroxidation, and oxidative stress.

In cases of coronary artery disease, the plant's root extract provided excellent prevention. Pre-treatment with root extract significantly reduced isoproterenol-induced oxidative stress. The numerous enzymes involved in lipid peroxidation, such as myocardial superoxide dismutase (SOD), catalase, and glutathione, block the outflow of myocyte creatine kinase-MB (CK-MB) and lactate dehydrogenase (LDH) enzymes. Those findings imply that the root extract has potent cardioprotective qualities.[69]

Conclusions

The findings presented here improve our understanding of herbal active chemicals and herbal composite formulae for the treatment and prevention of HCC. *Bauhinia variegata* Linn. and *Picrorhiza kurroa* have been identified as sources of active compounds with a wide spectrum of pharmacological activities, and have a high potential for driving the development of new remedies. They are widely used in the traditional healthcare system in India. They provide significant protection against a wide range of cancers, as well as other diseases.

Despite the fact that several studies have examined the anticancer effects and other qualities of these natural remedies, no cure for cancer has yet been discovered. Because of their anti-HCC and antioxidant properties, the plants presented in this review have anticancer potential. Finally, this article includes information on anticancer medicinal plants utilized across the globe. It is crucial that novel anticancer drugs produced from medicinal plants receive more research attention.

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