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Herbs with Hepatoprotective Effects on Liver- A Review

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Abstract

The well-being of your body as a whole depends on your liver. Liver disease and failure is a major issue in healthcare that impacts the pharmaceutical industry, government bodies charged with medication regulation, and medical professionals. The ways in which microorganisms, certain drugs used in chemotherapy, paracetamol, carbon tetrachloride, thioacetamide, and other potentially toxic substances might damage liver cells have been the subject of much study. The liver regulates a wide variety of bodily functions, making it a crucial organ. Chemicals enter and exit the body via a variety of pathways, some of which include metabolism, storage, release, and cleaning. These functions explain why liver illnesses continue to be a global health crisis, affecting individuals in every corner of the globe. The advancements in contemporary medicine have not yet resulted in a medication that can restore normal liver function, completely shield the organ from harm, or stimulate cell growth in the liver. A large body of scientific research has linked the beneficial benefits of some plants and fruits to chemical substances known as phytochemicals; these plants and fruits have a long history of medicinal usage.

KEYWORDS hepatoprotective, liver disease, herbal medications, Fruits.

Introduction

The liver is one of the most multipurpose organs in the body; it aids in digestion, produces chemicals, stores them, and eliminates any potentially dangerous ones. Worldwide, hepatic disorders continue to be a significant health concern and a leading danger to public health. The liver is responsible for a great deal of vital functions, and here is why. The leading cause of mortality and sickness in that area is liver cirrhosis, which is associated with 2.4% of all global fatalities. There are currently no effective medications that can restore liver cells, preserve the whole organ, or enhance liver function, despite the great strides made in contemporary medicine. Therefore, it is crucial to identify safer and more effective alternatives to medicines for liver illnesses by investigating plant-based alternatives. Plants produce phytochemicals via primary or secondary metabolism, and they are beneficial compounds or metabolites. Important for the plant's development and protection from other plants and pests, phytochemicals perform biological processes in the target plant. The nutrient-dense citrous fruits—including tangerines, grapefruits, lemons, limes, kiwis, and oranges—can aid in bodily health maintenance (Motawe et al., 2015). Natural therapies have a long history of success in treating liver illness, according to tests. A wide variety of substances may be derived from traditional medicines and nutraceuticals, which have been utilised by many people. Alkaloids, glycoside phenols, coumarins, essential oils, monoterpenes, vitamins, minerals, carotenoids, flavonoids, xanthenes, and countless other

compounds are often found in hepatoprotective foods and plants. In the health system, you may find several plant-based products. This dietary supplement and plant-based product has traditionally been used in conjunction with medication to alleviate hepatotoxicity. This research aims to learn more about the liver-protecting properties of natural products like botanicals and nutraceuticals.

LITERATURE REVIEW

Parveen Amana et al. (2022) Liver illnesses are a major issue in medicine worldwide, but they are disproportionately prevalent in underdeveloped nations. The most common culprits in triggering these symptoms are synthetic substances and, in extreme cases, overdoses of certain medications. Modern medicine has come a long way, but there is still no cure for liver disease, no medication that can prevent liver damage, and no treatment that can restore liver cells. Consequently, powerful medications are desperately needed to supplement or replace the ones that are already accessible. The diversity of plant life is crucial because it provides us with several novel medicinal compounds. This review compiles previous research on plant-based separations and synthetically defined particles that share a common ancestor and are able to shield the liver from harm. For example, A. paniculata and other species are included along with their groupings, locations of growth, sections utilised, types of tests performed, and ways in which they protect the liver in the research. Along with the correct chemical categories, it has 58 blends derived from higher plants. Helping researchers find common products that can cure liver problems is the purpose of this effort.

In 2014, Hassan Farghali studied The most promising plant active components for liver illness were the focus of this investigation. Both the scientific community and medical professionals examined these components. Most plant mixes containing these compounds cannot be recommended as a treatment for liver illness due to a lack of sufficient chemical data. In addition to providing a concise overview of popular models used in laboratory studies of potential hepatoprotective drugs, this article aims to showcase the most promising substances that have been tested in both people and laboratories. The process: A search for books was conducted using Google Search, PubMed, and the Web of Science (WOS). Here are the outcomes: By narrowing their emphasis to a small number of active components discovered in herbs, healthcare providers may identify hepatoprotective medicines supported by evidence. This may be accomplished by the use of computational chemistry to the study of molecular changes or pure chemical structures. Multiple processes in the pathobiology of the liver may be halted at one or more levels by natural hepatoprotective research, as shown in this review. To improve hepatotoxicity, for instance, these studies may halt oxidative stress on various levels, reducing reactive oxygen and nitrogen species. In conclusion, oral administration of plant medicines does not result in adequate absorption of their liver-protective components. Improving the bioavailability of these components is a goal of the research community. Parts of plants that are active when isolated or newly synthesised, structurally similar compounds should be the subjects of controlled, prospective, double-blind, worldwide trials. Because of this effort, more medications will be accessible to treat most liver diseases.

Saleh A. Almatroodi and colleagues (2020) studied Using in vitro and in vivo experiments, this research seeks to understand how garlic extract protects the liver. Garlic extract at a concentration of 600 εg/mL inhibited 67.5% of free radicals from causing cell damage and 71.36% of albumin denaturement, according to an in vitro research on antioxidant and anti-inflammatory potential. The animals were administered 150 µL of CCl4 (1:1 v/v in olive oil) orally to evaluate the hepatoprotective activity in real life. After that, they were given garlic extract (75 mg/kg b.w.) three times a week for eight weeks. The blood levels of Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), and Aspartate transaminaseas (106.7, 116.3, 136.4 U/L) were significantly lowered after administration of garlic extract in response to CCl4. Higher values (140.5, 156.2, 187.6 U/L) were seen in the disease control group. The levels of glutathione peroxidases (GPx), glutathione

(GSH), and superoxide dismutase (SOD) were shown to decrease considerably in rats that were exposed to CCl4. The corresponding concentrations were 29.3, 48.4, and 25.9 U/mg protein. An increase of 41.6, 63.3, and 32.5 U/mg protein, respectively, was seen in all measured antioxidant enzyme levels after treatment with garlic extract. Garlic extract administration was associated with decreased levels of many pro-inflammatory chemicals, according to this research (40.24, 460.4, 15.4, 45.14, and 125.3 pg/mL). The molecules in question were ICAM-1, Tumour necrosis factor-α, C-reactive protein (CRP), Interleukin-1β, and Interleukin-6. The levels in the group that was exposed to CCl4 were noticeably elevated. Changes such as cell invasion, edoema, and congestion were seen in animals that were exposed to CCl4. However, hepatocyte designs were improved in rats fed with garlic extract and CCl4. So, it seems that consuming garlic could be an excellent strategy to cure liver disorders, according to our research.

My name is Maulana. Alkandahri, Yusuf et al. (2023) The liver performs a plethora of critical functions, making it the body's most vital organ. The biochemistry and physiology of the organism may be altered by hepatic disorders. Hepatic disease occurs when the liver's cells, tissues, structures, and functions sustain damage. Cirrhosis and fibrosis are possible outcomes. Some of these conditions include hepatitis, alcoholic liver disease, nonalcoholic fatty liver disease, fibrosis of the liver, cirrhosis of the liver, hepatic failure, and hepatocellular carcinoma. Cell membrane rupture, immune system response, altered drug metabolism, accumulation of reactive oxygen species, peroxidation of lipids, and cell death are the hallmarks of liver disease. Despite significant advances in medical technology, no medication has yet been found that can restore liver function, shield it entirely, or stimulate cell growth. Furthermore, several medications might have negative side effects, hence herbal medicines are being selectively used as alternative treatments for liver illness. Many fruits, vegetables, and herbal remedies contain kaempferol, a form of pigment. Many diseases and conditions, including cancer, diabetes, and heart disease, are treated with it. Kaempferol has anti-inflammatory and antioxidant properties. It protects the liver in this way. The protective effects of kaempferol on the liver have been investigated in many hepatotoxicity models, including APAP-induced hepatotoxicity, acute liver damage (ALD), non-alcoholic fatty liver disease (NAFLD), CCl4, hepatocellular carcinoma (HCC), and lipopolysaccharide (LPS)-induced acute liver damage. Therefore, this paper aims to provide a concise summary of recent studies that have investigated the potential chemical mechanism of action of kaempferol and its capacity to protect the liver. Current knowledge on the chemical composition, natural source, bioavailability, and safety of kaempferol is also included.

Bipindra Pandey and colleagues (2023) Historical Context Natural bioactive components derived from secondary metabolites in plants have shown promise in animal studies for the prediction and amelioration of hepatotoxicity and its consequences. The primary objective of this study is to provide an overview of the current medications used to treat liver disease and the methods used to assess the potential protective effects of important phytoconstituents. It will also discuss the mechanisms of action and clinical studies of some natural medicines that show promise in treating various liver ailments. Central text In this study, we will look at fifteen important phytoconstituents that have been identified. We will also go over their biological origins, chemical structures, plant parts utilised, extract type, hepatoprotective test technique, and potential roles in liver protection. We provide a brief overview of nine natural hepatoprotective leads, discussing their structures and how they protect the liver. The study also discusses the outcomes of current clinical studies with various hepatoprotective leads and their efficacy in treating liver disease. The primary mechanism by which phytoconstituents inhibit many disease processes is their antioxidant characteristics, according to scientists. They do this by enhancing cellular antioxidant defences, eliminating free radicals, decreasing lipid peroxidation, raising anti-inflammatory

potential, and strengthening protection against liver cell damage. This review discusses the most recent developments in the synthesis of hepatoprotective leads from natural materials and their potential use in the treatment of various liver diseases. Natural hit and lead molecules are also thought to be useful in the search for novel therapeutic compounds and in mitigating side effects of liver-damaging pharmaceuticals and industrial toxins. To completely comprehend the biological action of these chemical compounds derived from natural sources, more research is required. Because of this, pharmaceutical companies will be able to develop better hepatoprotective regimens in the future.

HEPATOPROTECTIVE NATURAL PRODUCTS

Thanks to the efforts of major pharmaceutical corporations, herbal remedies for liver issues, which have a long history of usage in India, have gained popularity globally. Despite the widespread use of herbal remedies for a range of ailments, including liver issues, these methods are not appropriate. Thus, there has been a lot of investment in the development of liver-protective pharmaceuticals derived from plants on a worldwide scale. Many herbs and combinations supposedly offer liver-protecting properties. Some 110 plants have 160 phytoconstituents that have liver-protective properties. More than 87 plants are used to create 33 distinct and confidential multi-ingredient plant combinations in India. Modern medicine has come a long way, yet there are currently no effective and safe hepatoprotective medications on the market. This is why developing hepatoprotective medications derived from plants to treat various liver illnesses has gained global significance. The purpose of this study is to compile data from published research on medicinal plant phytochemicals that have been tested in hepatotoxicity models and have shown potential. The purpose of this literature review is to compile data from investigations on the effects of medicinal plant phytochemicals on hepatotoxicity models. Indica, Azadirachta, Andrographis, Curcuma, Phyllanthus, Foeniculum vulgare, Swertia, Picrorhiza, kurroa, Flacourtia, Wedelia, calendulacea, Aegle marmelos, and Prostechea are all known to have liver-protective properties.

Solanum nigrum

Mice with thioacetamide (TAA)-induced liver fibrosis were given Solanum nigrum extract (SNE). Throughout the experiment, pure water and SNE (0.2 or 1.0 g/kg) were given to mice in all three TAA groups every day through a gastrostomy. In TAA-treated mice, SNE lowered the amounts of hydroxyproline and α-smooth muscle actin proteins in their livers. The liver's collagen (α1) (I), transforming growth factor-β1 (TGF-β1), and mRNA levels were all lowered by SNE. TAA treatment caused more fibrosis, but SNE lessened it, according to a histological study. Ingesting SNE greatly lowers the liver scarring caused by TAA in mice, most likely by lowering the release of TGF-β1.

In a different study, the water extract of SN (ASNE) was tested to see if it could protect rats' livers from damage caused by CCl4. The results showed that treating the rats with ASNE greatly reduced the amounts of liver enzyme markers, superoxide, and hydroxyl radicals in their blood that were caused by CCl4. Histopathology of the liver showed that ASNE decreased the number of liver lesions caused by CCl4 in rats. These lesions included hepatic cells cloudy swelling, lymphocytes invasion, hepatic necrosis, and fibrous connective tissue growth. The study's results show that ASNE may be able to protect the liver from CCl4-induced oxidative damage in rats. It is possible that this liver-protecting effect is due to its ability to change detoxification enzymes and its antioxidant and free radical scavenging properties (Lin et al., 2008). The plant extracts of Solanum nigrum and Cichorium intybus, which are mixed with calf thymus DNA and a method for making free radicals, protect the DNA's deoxyribose sugar portion from oxidative damage. The result depended on how much plant juice was used. There was a big difference between the effects of Cichorium intybus and Solanum nigrum, though. These studies suggested that the hepatoprotective effect of these raw plant extracts might be because they stop DNA in tissue waste from being broken down by oxygen. Since these plants are known as hepatoprotective drugs and have been shown to protect against CCl4-

induced liver damage, it is possible that their effectiveness is due to their ability to remove free radicals.

Azadirachta indica

A. indica leaf (meliaceae) extract was tested on blood enzyme levels (glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acid phosphatase, and alkaline phosphatase) that were raised by paracetamol in rats. This was done to see if this plant might have any liver-protecting properties. It says that the group that was treated with the extract was safe from the damage that paracetamol did to liver cells. A histopathological study of the liver added to the proof of the results. It's likely that picroliv's ability to protect the liver from damage is because it changes the way harmful substances are broken down in the body, which leads to fewer reactive chemicals being made.

Andrographis paniculata

The antihepatotoxic action of the plant's methanolic extract (equivalent to 100 mg/kg of andrographolide) and 761.33 mg/kg ip of the andrographolide-free methanolic extract (equivalent to 861.33 mg/kg of the methanolic extract) was tested on rats that had been given CCl4. To figure out how well the liver was working, biochemical markers such as serum alkaline phosphatase, serum bilirubin, serum transaminases (GOT and GPT), and hepatic lipids were measured. The data show that andrographolide is the main active ingredient in A. paniculata that is harmful to the liver.

Flacourtia indica

We tested products from the upper parts of Flacourtia indica (Burm.f.) Merr to see if they could protect the liver. All of the products were able to lower the levels of serum aspartate transaminase (AST), serum alanine transaminase (ALT), and serum alkaline phosphatase (ALP) in rats that had liver damage caused by paracetamol. The serum levels of AST and ALT dropped the most when the petroleum ether and ethyl acetate extracts were given orally at a dose of 1.5g/kg of body weight. The petroleum ether extract dropped the levels of AST by 29.0% and ALT by 24.0%, while the ethyl acetate extract dropped the levels of AST by 10.57% and ALT by 6.7% compared to animals that were given paracetamol (3 g/kg of body weight). The histopathological study also showed that the petroleum ether and ethyl acetate extracts helped the paracetamol-induced necrosis get better. However, the methanol extract did not have a noticeable impact on the liver damage caused by paracetamol. That petroleum ether and ethyl acetate extract can protect the liver might be because they stop microsomal drug-metabolizing enzymes from working. But the amount they used in this study was too high, and it doesn't make sense for a human dose.

Aegle marmelos

The Indian System of medicine used the leaves of the aegle marmelos plant, which is in the family Bael and the genus Bilva. Bulva was an old Sanskrit word for the plant. The liver-protecting effect of Aegle marmelos was tested on rats with liver damage caused by alcohol using important biochemical markers. The results showed that the Bael leaves are very good at protecting the liver. Other workers also came to the same conclusions.

HEPATOPROTECTIVE FRUITS

Grapefruit (Citrus paradisi)

Overview: As a part of the Rutaceae family and the genus Citrus, the grapefruit is an important plant. Its formal name is Citrus paradisi. The grapefruit was first grown on the island of Barbados. It is now grown in Mexico, Spain, Morocco, Israel, Jordan, South Africa, Brazil, Jamaica, and Asia. It is eaten as a seasonal fruit or in juice with other foods. In many countries, it has also been used in traditional and common medicine as an antibacterial, antifungal, anti-inflammatory, antioxidant, and antiviral, as well as an astringent, and as a preserve. Over the past few decades, studies have shown that grapefruit may help with regenerating cells, lowering cholesterol, cleansing the body, keeping the heart healthy, managing rheumatoid arthritis, keeping weight in check, and preventing cancer. Grapefruit juice is a great way to get a lot of phytochemicals and nutrients that are good for you. A lot of vitamin C, folic acid, phenolic acid, potassium, calcium, iron, limonoides, terpenes, monoterpenes, and D-glucaric acid are found in it. Beta-carotene and lycopene are antioxidants that can be turned into vitamin A by the body. The red and pink types also have these compounds. But naringin,

which people break down into naringenin, is the flavonoid that is most concentrated.

Hepatoprotective evidence for naringin and naringenin: However, even though grapefruit is often eaten raw or in juice, there have been no studies that directly look at how it protects the liver from damage caused by hepatotoxic chemicals. A study of naringenin and naringin has given us the most convincing proof that it may help protect the liver.

In one of the first studies, Parmar looked at how blocking histidine decarboxylase could help ulcers in rats. He looked at retention ulcers and pyloric ligatures caused by phenylbutazone and aspirin. The researchers found that naringenin significantly reduced mucosa damage in both models, with the protective effect being stronger in ulcers with pyloric ligation. This suggests that naringenin worked by stopping the production and release of endogenous histamine in rats' gastric mucosa.

These findings led to more research into hepatoprotective benefits. For example, in 2004, researchers looked into how naringenin could protect rats' livers from damage caused by dimethyl nitrosamine (DMN). Giving naringenin (20 and 50 mg/kg everyday for 4 weeks) by mouth greatly reduced the damage caused by DMN. This was seen in the liver's weight, as well as levels of alanine transaminase (ALAT), aspartate transaminase (ASAT), alkaline phosphatase (ALP), and jaundice. Naringerin also brought back the normal amounts of proteins in the blood, albumin, and liver malondialdehyde (MDA). The results showed that naringenin could stop the growth of fibrin and protect the liver, which means it might be useful in treating hepatic fibrosis.

According to Seo et al., the only study that found proof that naringin could protect the liver was their study on how a naringin substance affected the control of fat and ethanol metabolism in male Sprague-Dawley rats. The animals were put into six groups based on the types of food they were given: ethanol- and naringin-free; ethanol (50 g/L) plus low-naringin (0.05 g/L); ethanol plus high-naringin (0.125 g/L); and three groups that were fed equivalent amounts of each. Couple-fed control rats got an equal-calorie meal for 5 weeks that had dextrin-maltose instead of ethanol. Adrenaline boosters greatly dropped the amount of ethanol in the plasma of the ethanol-treated groups while simultaneously raising the activity of ADH and/or ALDH. Notably, adding naringin to the ethanol-treated groups lowered liver triglycerides (TGs) and plasma and hepatic total cholesterol (TC) significantly compared to the naringin-free group. Increased naringin levels greatly raised HDL cholesterol and the HDL-c/TC ratio, while decreasing AI levels in the ethanol-treated groups. Within the ethanol-treated groups, hepatic fat formation was also significantly lower in the naringin-added groups compared to the naringin-free groups. However, there were no changes observed between the pair-fed groups. Low-naringin intake significantly lowered the amounts of TBARS in the plasma and liver, while increasing SOD and GPx functions and glutathione (GSH) levels in the liver. Neringin seems to help lessen the bad effects of drinking alcohol by improving the breakdown of ethanol and lipids and strengthening the liver's antioxidant defense system.

Grape (Vitis vinifera L)

Overview: The grape, whose formal name is Vitis vinifera, is a woody climber plant that can grow up to 30 m tall when left to grow naturally. However, people prune it every year, so it stays a small, 1-m bush most of the time. Grapes are fruits that grow on vines. You can eat them, and they are used to make wine and other alcoholic drinks. Viticulture started in Asia and Southeastern Europe. Because of this, the grape has become an important part of human nutrition, and its farming has spread to the American and African continents. There are about 3000 different kinds of grapes in the world, but not all of them are liked the same way. Grapes are divided into two main groups based on what they are used for: (1) table grapes, which are meant to be eaten with food, and (2) wine grapes, which are used to make wine. Both the fruit and the leaves are very high in vitamins, minerals, and other active ingredients (Table 1). These ingredients have been linked to medical qualities, which is why some authors have called the grape a drug-food. From different parts of this plant,

Table 1: Main active ingredients of the grape

Active ingredient	Compounds
Carbohydrates	Glucose, fructose, sacarose, dextrose, yeast, and levulose
Vitamins	Vitamin C and vitamin B_6
Beta-carotene	Vitamin A
Tannins	Resveratrol
Minerals	Potassium, magnesium, calcium, sulfur, iron, and manganese
Flavonoids	Quercetin

Many different preparations, mostly from the fruit, have been used in traditional and popular medicine. These include laxatives, astringents, diuretics, wound healers, immunological stimulants, anti-inflammatory drugs, low-cholesterol drugs, and chemopreventatives against heart disease and some cancers (mostly prostate and colon).

CONCLUSION

In this review piece, information about a few natural goods that protect the liver has been gathered and put together. This will help people who want to try alternative medical systems. A more in-depth look at the different plant goods sold in India and other countries that protect the liver will be coming soon. The current study put together the best proof for how some fruits and plants, a natural glue, and one of the main carbohydrates found in the cell walls of yeasts, algae, and grains protect the liver from harmful chemicals. Similarly, the studies showed that using fruits and plants in traditional medicine to protect against liver damage is a good way to treat chronic degenerative illnesses. The mentioned plants, fruits, and chemicals might provide new ways to treat liver diseases compared to the few treatments that are currently available. This means that these foods should be looked at in future research.

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