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Review Article

Review of Natural Products with Hepatoprotective Effects on Liver

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Abstract

Ensuring that your liver stays healthy is very important for your general health. A big problem in health care is liver damage or liver failure, which affects not only doctors but also the drug business and the agencies that regulate drugs. A lot of research has been done on how bacteria, certain antibiotics, chemotherapy agents, paracetamol, carbon tetrachloride, thioacetamide, and other harmful chemicals can hurt liver cells. One of the most important parts in the body is the liver, which controls many different processes. These include the metabolism, release, storage, and cleansing of chemicals from inside and outside the body. Because of these roles, liver diseases are still one of the biggest threats to public health, and people all over the world still have problems with them. Even though modern medicine has come a long way, there are still no fully effective drugs that can improve liver function, fully protect the organ, or fully help liver cells grow back. Some plants and fruits have been used for health reasons for a long time, and many scientific studies have shown that the good effects of these plants and fruits come from chemical compounds called phytochemicals.

Keywords hepatoprotective, liver disease, herbal medications, Fruits

Introduction

As one of the body's most important parts, the liver does many things, including breaking down food, releasing chemicals, storing them, and getting rid of harmful ones. Hepatic diseases are still one of the biggest threats to public health and a major health issue around the world. This is because the liver does so many important things. Liver cirrhosis, which is linked to 2.4% of all deaths in the world, is the main cause of death and illness in that region. Even though modern medicine has come a long way, there are still no fully successful drugs that improve liver function, protect the whole organ, or help liver cells grow back. Finding plant-based replacements to pharmaceuticals that treat liver diseases is therefore very important if we want to find better and less dangerous options. Phytochemicals are useful chemicals or metabolites that come from plants and are made by either primary or secondary metabolism. The phytochemicals do biological things in the target plant and are very important for its growth and defense against pests, diseases, and other plants.

Citrus fruits like oranges, grapes, lemons, lime, kiwis, and tangerines are chock full of nutrients that can help your body stay healthy (Motawe et al., 2015). Plus, there is a long history of experiments showing that natural medicines can help treat liver disease. Many people have used traditional medicines and nutraceuticals, and these have a lot of different ingredients that can be extracted. Hepatoprotective foods and plants usually have many different chemicals in them, such as alkaloids, glycoside phenols, coumarins, essential oils, monoterpenes, vitamins, minerals, carotenoids, flavonoids, and xanthenes. There are a lot of plant products in the health system.

Typically, this plant-based product and dietary supplement has been used with medicine to treat hepatotoxicity. The goal of this study is to look into how natural products, such as plants and nutraceuticals, can protect the liver.

LITERATURE REVIEW

Amana Parveen et.al (2022) Liver diseases are a big problem in medicine generally, and they're especially common in developing countries. The main things that cause them are manufactured drugs and some medicines that are taken in very large amounts. Even with all the progress in modern medicine, there is still no effective medicine that can increase liver function, protect the liver from damage, or help liver cells grow back. As a result, there is an urgent need for strong medicines to replace or add to the ones that are already available. Plant life is definitely important because it gives us a lot of new medicines. This study looks at what has been written about plant-based separations and synthetically defined particles that all have the same starting point and can protect the liver. The study lists different plants, their groups, where they grow, what parts of the plants are used, what kind of tests were done, and how they protect the liver, for example A. paniculata and some other species. It also has 58 mixes that were extracted from higher plants and put into the right chemical groups. The goal of this work is to assist scientists in their search for common things that can help treat liver diseases.

Hassan Farghali et.al (2014) In this study, we looked at some plant active ingredients that were thought to be the most hopeful for liver disease. These ingredients were looked at from both a basic science and a clinical point of view. Because there isn't enough chemical information, most plant mixtures that contain these molecules can't be suggested as a way to treat liver disease. The goal is to show the most hopeful compounds that have been tried in both labs and humans, as well as to briefly talk about common models used in lab tests of possible hepatoprotective compounds. How it works: It was done a book search using Web of Science (WOS), PubMed, and Google search. The results are: Health workers working in treatments can find evidence-based hepatoprotective agents by focusing on a few key active ingredients found in herbs. This can be done by studying pure chemical structures or molecular changes using computational chemistry. This review shows that natural hepatoprotective studies can stop multiple processes in the liver's pathobiology at one or more levels. For example, these studies can stop oxidative stress at multiple levels to lower reactive oxygen and nitrogen species, which makes hepatotoxicity better. Conclusion: The liver-protecting parts of plant medicines are not well absorbed when taken by mouth. Researchers are working on ways to make these parts more bioavailable. Controlled prospective double-blind international studies should be done on plant parts that are active when separated or on related new molecules that have had their structures changed. This work will lead to more drugs being available for the vast majority of liver illnesses.

Saleh A. Almatroodi et.al (2020) The current study aims to find out how garlic extract protects the liver by doing tests both in living things and in test tubes. The in vitro study of antioxidant and anti-inflammatory potential showed that 600 εg/mL of garlic extract could stop 67.5% of free radicals from damaging cells and 71.36% of albumin from becoming denatured. In order to study the hepatoprotective action in real life, 150 µL of CCl4 (1:1 v/v in olive oil) was given orally to the animals, and they were then given garlic extract (75 mg/kg b.w.) three times a week for eight weeks. Giving garlic extract greatly reduced the rise in serum Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), and Aspartate transaminaseas (106.7, 116.3, 136.4 U/L) caused by CCl4. This was compared to the disease control group, which had higher levels (140.5, 156.2, 187.6 U/L). Superoxide dismutase (SOD), Glutathione peroxidases (GPx), and Glutathione (GSH) levels dropped significantly in animals that were exposed to CCl4. These levels were 29.3, 48.4, and 25.9 U/mg protein, respectively. Also, treating with garlic extract led to a big rise in the levels of all the antioxidant enzymes that were tested (41.6, 63.3, and 32.5 U/mg protein, in that order). This study also found that the levels of a

number of pro-inflammatory molecules (40.24, 460.4, 15.4, 45.14, and 125.3 pg/mL) went down after the garlic extract treatment. These molecules were Tumor necrosis factor-α, C-reactive protein (CRP), Interleukin-1β, Interleukin-6, and ICAM-1. The levels of CCl4-induced group were significantly higher. Animals that were introduced to CCl4 had changes like cell invasion, swelling, and congestion. On the other hand, animals that were treated with garlic extract and CCl4 had better hepatocyte designs. So, our results support the idea that eating garlic may be a good way to treat liver problems.

Maulana Yusuf Alkandahri et.al (2023) The liver is the most important organ in the body and does many important things. Hepatic diseases can change how the body's biochemistry and physiology work. When cells, tissues, structures, and processes of the liver are damaged, this is called hepatic disease. This can lead to fibrosis and eventually cirrhosis. Hepatitis, ALD, NAFLD, liver fibrosis, liver cirrhosis, hepatic failure, and HCC are some of these diseases. Liver diseases happen when cell membranes break, the immune system reacts, drug metabolism changes, reactive oxygen species build up, lipids peroxide, and cells die. Even though modern medicine has come a long way, there is still no drug that can improve liver function, protect it completely, and help liver cells grow back. Additionally, some meds can have bad side effects, and herbal remedies are being carefully chosen as new ways to treat liver disease. Kaempferol is a type of pigment that can be found in many fruits, veggies, and herbal medicines. We use it to take care of many illnesses, like diabetes, heart disease, and cancer. Kaempferol is a strong antioxidant that also reduces inflammation. Because of this, it protects the liver. Previous studies have looked at how kaempferol protects the liver in a number of different hepatotoxicity models, such as APAP-induced hepatotoxicity, ALD, NAFLD, CCl4, HCC, and lipopolysaccharide (LPS)-induced acute liver damage. So, the goal of this report is to give a quick review of current research on kaempferol's ability to protect the liver and its possible chemical method of action. It also has the newest research on kaempferol's chemical makeup, where it comes from naturally, how bioavailable it is, and how safe it is.

Bipindra Pandey et.al (2023) Background Information Experiments have shown that natural bioactive components generated from plant secondary metabolites are good options for predicting and easing the effects of hepatotoxicity and its long-term problems. This review's main goal is to explain the modern medicines that are commonly used to treat liver disease and how major phytoconstituents have been tested for their ability to protect the liver. It will also talk about how some promising natural agents work and how they have been used in clinical trials to treat people with different liver diseases. Primary text This review shows fifteen main phytoconstituents that have been isolated, along with their biological sources, chemical structures, the plant parts that were used, the type of extracts that were used, the hepatoprotective test method that was used, and how they might work to protect the liver. We quickly talk about nine potential hepatoprotective leads that come from natural sources, including their structure and how they work to protect the liver. In addition, the review talks about the results of recent clinical trials of some hepatoprotective leads and how they worked with different liver disease patients. Scientists have found that antioxidant properties are the main way that phytoconstituents stop different disease pathways. They do this by boosting the antioxidant defense system of cells, removing free radicals, lowering lipid peroxidation, increasing anti-inflammatory potential, and protecting liver cell injury even more. This review talks about the latest progress in making hepatoprotective leads from natural products and how they might be able to cure different types of liver illnesses. Moreover, it is assumed that hit and lead molecules derived from natural sources can be used to find new drug molecules and reduce the problems caused by medications and chemicals that damage the liver. More study should be done to fully understand how these natural-based chemical agents work on a biological level. This will help the

pharmaceutical industry come up with more useful hepatoprotective regimens in the future.

HEPATOPROTECTIVE NATURAL PRODUCTS

Herbal treatments for liver problems have been used for a long time in India and have become popular around the world thanks to big drug companies. While many people use plant medicines for a variety of reasons, including liver problems, they are still not acceptable ways to treat these conditions. So, the global market has put a lot of effort into making drugs from plants that protect the liver. There have been claims that a lot of plants and mixtures can protect the liver. It is said that about 160 phytoconstituents from 101 plants can protect the liver. To make 33 unique and secret multi-ingredient plant mixtures in India, more than 87 plants are used. Even with all the great progress that has been made, there are still no important and safe hepatoprotective drugs available in modern medicine. For this reason, it has become very important around the world to create plant-based hepatoprotective drugs that can treat a wide range of liver diseases. This review aims to gather information from published studies on phytochemicals from medical plants that have shown promise and have been tried in hepatotoxicity models. The goal of this review is to gather information from published studies on phytochemicals from medical plants that have shown promise and have been tried in hepatotoxicity models. The liver-protecting effects of Solanum nigrum, Curcuma longa, Phyllanthus emblica, Foeniculum vulgare, Swertia Chirata, Picrorhiza kurroa, Azadirachta indica, Andrographis paniculata, Flacourtia indica, Wedelia calendulacea, Aegle marmelos, and Prostechea michuacana are seen.

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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