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Review Article

Roles of Herbals in Paracetamol Induced Hepatotoxicty

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Abstract

In the area of herbal medicine, this has led to a great deal of research and development. In the majority of industrialized and developing nations today, there is a rising need for herbal medicine. The most common form of liver disease varies by country and may be impacted by local factors. Infection with viruses and exposure to specific chemicals are two causes of liver diseases. Herbal medications have the potential to be an effective treatment for liver problems. An extensive review of the literature on hepatoprotective plants clearly shows that herbal medications have significant promise for the treatment of liver ailments. It is difficult to find effective treatments for common liver conditions such as cirrhosis, fatty liver, and chronic hepatitis. There aren't many therapeutic drugs that work well and rarely cause side effects. Few plants can effectively treat liver disorders, so there is a lot of interest in researching the many plant therapies that can help with liver diseases. As a result, we conclude that herbs are an important source of hepatoprotective and liver regeneration drugs. More study is needed, however, to identify, characterize, and standardize the active substances, beneficial compounds, and formulations for the treatment of liver illnesses. The availability of modern hepatoprotective medications with realistic clinical utility is still quite restricted, and the discovery of new compounds with similar potentials will undoubtedly encourage the drug discovery process.

Keywords: Herbal Medicine, Hepatotoxicity, Hepatoprotective, Antioxidant Activities

Introduction

Many contemporary medications have been proven to have negative side effects on the human body despite being mostly based on synthetic chemical substances. In the area of herbal medicine, this has led to a great deal of research and development. In the majority of industrialized and developing nations today, there is a rising need for herbal medicine.[1] The most common form of liver disease varies by country and may be impacted by local factors. Infection with viruses and exposure to specific chemicals are two causes of liver diseases. An important health issue is a chemical that damages the liver cells in some individuals and results from substantial liver damage brought on by medications and by the concoction of pharmaceuticals and other substances. It is difficult to find effective treatments for common liver conditions such as cirrhosis, fatty liver, and chronic hepatitis.[2] Effective therapeutics with few adverse effects are needed by patients and doctors. There aren't many therapeutic drugs that work well and rarely cause side effects. Few plants can effectively treat liver disorders, so there is a lot of interest in researching the many plant therapies that can help with liver diseases.[3] The present review is aimed at compiling the data on promising herbal extracts from the plant that have been tested in the hepatotoxicity model using the modern scientific system.

The liver is the body portion with the highest rate of metabolic activity in addition to being the largest organ in terms of size. One of the most important organs, it serves as a common hub for nutrient metabolism, digestion, product storage, and excretion. Additionally, the liver plays a crucial role in the metabolism of drugs and the elimination of xenobiotics from the body, protecting the body from foreign chemicals by detoxifying and removing them. Hepatic toxicity may result from some compounds like CCL4, PCM used in laboratories, lead, and arsenic used in industries, or naturally occurring poisons (microcystins).[4] A study found that 50% of all hospitalizations and 50% of all cases of acute liver failure are due to drug-induced hepatic toxicity. One of the most frequent reasons why drugs are taken off the market is drug-induced hepatotoxicity.[5] Liver damage is also brought on by metabolic syndrome (which includes obesity, diabetes, hypertension, and hyperlipidemia), insulin resistance, alcohol use, and oxidative stress.[6] Hepatocytes are damaged by these hepatotoxic agents, which also activate the innate immune system and result in the production of pro-inflammatory markers such as TNF, IL, and gamma interferon (Fig. 1).[6,7]

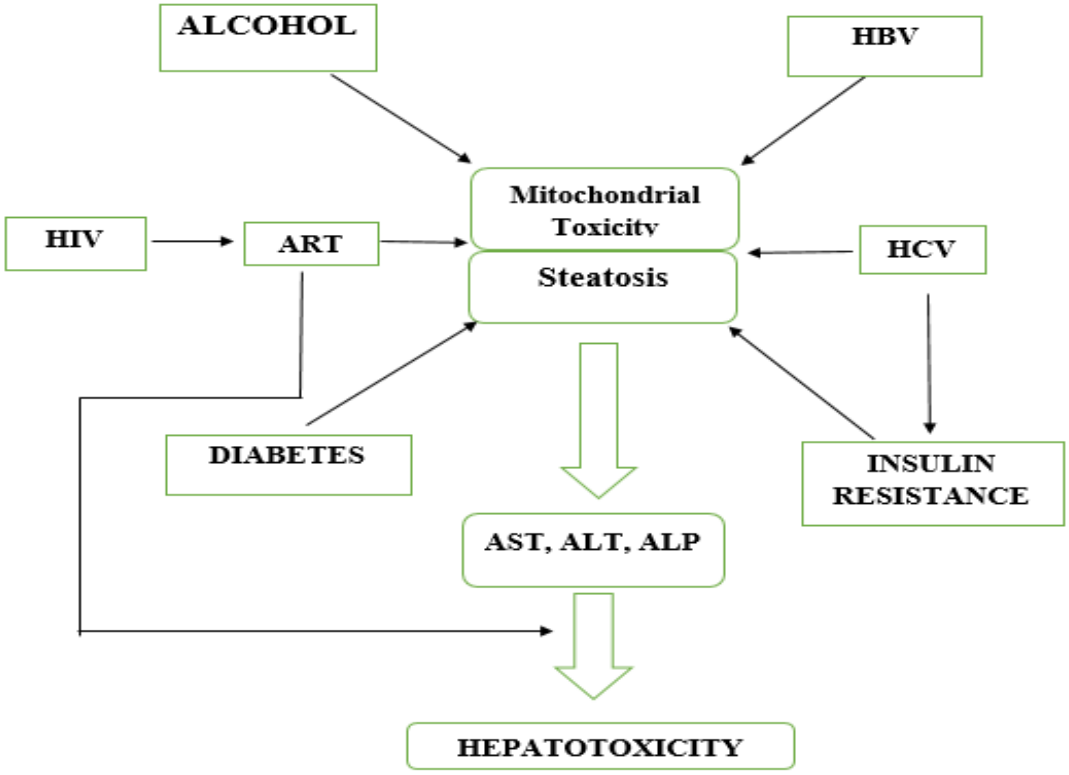

Figure 1: Induction of hepatotoxicity by various agents.

Some hepatotoxic substances frequently cause mitochondrial damage, which inhibits the electron transport pathway and results in oxidative stress. The antipyretic and analgesic medication paracetamol (PCM), which is frequently used for medical and therapeutic purposes, is also known to cause liver damage. The function and morphology of the liver mitochondria were reported to have been changed by hazardous doses of PCM in various investigations.[8] The substances known as hepatoprotective agents lessen liver damage brought on by hepatotoxic substances. Alcohol, CCl4, beta galactosamine, thioacetamide (TAA), paracetamol (PCM), nimesulide, anti-tubercular medications like isoniazid, rifampicin, and other substances that cause hepatotoxicity in rats and mice are used to study the hepatoprotective effects of plant medicines and herbal formulations.[9] Herbs are crucial in the treatment of a variety of liver problems because allopathic medicine lacks effective liver-protecting medications. However, numerous native plants have been employed in Ayurveda as hepatoprotective agents. Many native plants, though, have been used in Ayurveda as hepatoprotective remedies.[10] The utilization of plant materials is a major component of Indian traditional medicine such as Ayurveda, Siddha, and Unani. Because of their efficacy, safety, and affordability, herbal medications have grown in importance and appeal in recent years. In some circumstances, the relationships that medicinal plants have with other plants in their habitat have an impact on their medical efficacy. The hepatoprotective properties of plant products are one of its significant and well-established uses. Consequently, safe hepatoprotective medication is constantly needed.[11] Natural treatments for liver illnesses have a long history, and they are still employed in some capacity worldwide in the form of medicinal plants and their derivative.[10] Scientific analysis of plants has frequently demonstrated that their active principles are what make treatments effective. Many medicinal plants have been tested, and it has been discovered that many of them contain active ingredients with healing effects for a wide range of illnesses.[12] Numerous chemical components, including phenols, coumarins, lignans, essential oils, monoterpenes, carotenoids, glycosides, flavonoids, organic acids, lipids, and alkaloids, are present in liver-protective plants.[13]

Hepatoprotective Herbs

Leading pharmaceutical companies have helped make herbal-based treatments for liver problems popular all over the world. They have been used for a long time in India to treat liver disorders. Even though many herbal remedies are extremely popular overall and for treating liver illnesses in particular, they are still unsuitable therapy options.[14] The impediments to this inevitability include (i) the lack of standardization of herbal treatments; (ii) the inability to identify the active ingredient(s) or principle(s); (iii) the absence of randomized controlled clinical trials (RCTs); and (iv)the absence of toxicological examination. Natural liver disease treatments have a long history, dating back to the Ayurvedic system and extending to the Chinese, European, and other traditional medical systems.[15] In the 21st century, there has been a paradigm shift towards the therapeutic evaluation of herbal products in liver disease models by carefully combining the benefits of traditional medical systems with the contemporary concept of evidence-based medicinal evaluation, standardization, and randomized placebo-controlled clinical trials to support clinical efficacy.[16] Hepatoprotective properties of numerous plants and formulas have been asserted. It has been asserted that around 160 phytoconstituents from 101 plants have liver-protective properties. 33 patented and unique multi-ingredient plant compositions contain more than 87 plants from India.[10] Despite the enormous progress gained, there are still no substantial and safe hepatoprotective drugs used in modern treatments.[16] The development of plant-based

hepatoprotective medicines that are effective against a range of liver illnesses has therefore received the proper attention on a global scale. The role of medicinal plants is crucial since they not only preserve human and animal health and vigor but also treat several diseases, such as liver disorders, without posing any danger to humans or other animals. India, which is aptly referred to as the "Botanical Garden of the World," is the world's largest producer of medicinal herbs.[17] The purpose of this study is to gather information about promising phytochemicals from medicinal plants that have been studied in hepatotoxicity models based on published studies.

Table 1: List of Some Hepatoprotective Plants.

S No.	Name of Plant	Family	Parts Used	Active Principle	Ref
1.	*Abrus cantoniensis*	*Leguminoceae*	Whole plant	Soyasaponin I, Kaikasaponin III, Triterpenoidal, Saponins	18
2.	*Abutilon indicum*	*Malvaceae*	Fruit	Luteolin, chrysoeriol, Luteolin 7-O-β- glucopyranoside, chrysoeriol 7-O-β- glucopyranoside	19
3.	*Acacia catechu*	*Leguminoceae*	Heartwood	Catechins	20
4.	*Acacia ferruginea*	*Fabaceae*	Leaf	Total Phenolic content, Flavonoids, Saponins	21, 22
5.	*Achillea millefolium*	*Asteraceae*	Seeds, whole plant	Flavonoids, Apigenin, Quercetin	23
6.	*Achyranthes aspera*	*Amaranthaceae*	Aerial plant	20-hydroxyecdysone, quercetin-3-O-β-D-galactoside	24
7.	*Aegle marmelos*	*Rutaceae*	Leaf	Alkaloids, Coumarins	25
8.	*Aloe barbadensis*	*Liliaceae*	Leaf	Anthraquinones	26
9.	*Ananas cosmos*	*Bromeliaceae*	Leaf	Bromelain	27
10.	*Andrographis paniculata*	*Acanthaceae*	The whole plant, leaf	Diterpenoids, Andrographolide, Andrographiside, Neoandrographoiide	28
11.	*Aphanamixis polystachia*	*Maliaceae*	Bark	Poriferasterol-3-rhamnoside	29
12.	*Apium graveolens*	*Umbelliferae*	fruit	Essential Oil	30
13.	*Arctium lappa*	*Compositae*	Root	Alkaloids, Flavonoids	30
14.	*Argemone maxicana L.*	*Papaveraceae*	Seed	Essential Oil	31
15.	*Asterocantha longifolia*	*Acanthaceae*	Leaf	Alkaloids, Steroids, Tannins, Flavonoids	32
16.	*Alstonia scholaris*	*Apocyanaceae*	Bark	Flavonoidal glycosides, indole, and other alkaloids	33
17.	*Adhatoda vasica*	*Acanthaceae*	Leaf	Vasicine, alkaloids l-vasicinone, deoxyvasicine, maiontone, vasicinolone and vasicinol	34
18.	*Annona squamosa*	*Annonaceae*	Leaf	Alkaloids, Glycosides, Corticosteroids, Essential oil	35
19.	*Argyrolobium roseum*	*Papilionaceae*	Whole plant	Flavanoid glycoside	36
20.	*Artemisia mendozana DC.*	*Asteraceae*	Leaf, Flower, shoot	Flavonoids, Tannins	37
21.	*Auxemma oncocalyx*	*Boraginaceae*	Whole plant	Quinone fraction	38
22.	*Azadirachta indica*	*Meliaceae*	Leaf	Quercetin-3-O-β-D glucoside, Myricetin -3-O-rutinoside, Quercetin-3-O-rutinoside, Kaempferol-3-O-rutinoside	39
23.	*Balanites aegyptiaca*	*Zygophyllaceae*	Leaf	Alkaloids, Flavonoids, Glycosides, Phenols, Saponins, Tannins	40
24.	*Baliospermum montanum*	*Euphorbiaceae*	Root	Phenolic And Flavonoid Compounds	41
25.	*Baeckea frutescens*	*Myrtaeeae*	Essential oil	1, 8 cineol, p-cymene, a-pinene. Alkaloids	42

26.	*Bauhinia variegata*	*Caesalpiniaceae*	Root	Flavonoids, Triterpenes, Tannins, and Steroids	43
27.	*Bauhinia purpurea*	*Caesalpiniaceae*	Leaf, unripe pod	Flavonoids, Triterpenes, Tannins, and Steroids	44
28.	*Berberis aristata*	*Berbaridaceae*	Root, bark, berry, leaf	Berberine	45
29.	*Berberis lycium Royle*	*Berbaridaceae*	Leaf	Barberin, Barbamine	46
30.	*Boerhaavia diffusa*	*Nyetaginaceae*	Whole plant	9,10- dimethyl-4- methoxyrotenoid	47
31.	*Bryophyllum pinnatum*	*Crassulaceae*	Leaf	8α-oleanane, ψ-taraxasterol, α- and β-amyrins	48
32.	*Bupleurum falcatum*	*Umbellifera*	Seed	Saikosaponins	49
33.	*Butea monosperma Lam.*	*Fabaceae*	Stem	Quercetin, Buteasperamin B	50
34.	*Capparis spinosa*	*Capparidaceae*	Root, bark	Bioactive lipids, glucosinolates flavonoids, seed oil	51
35.	*Cassia fistula*	*Leguminoceae*	Leaf	Steroids, triterpenoids, anthraquinone	52
36.	*Cassia angustifolia Vahl.*	*Leguminoceae*	Leaf	Piperidine alkaloids, anthracene derivatives	53
37.	*Cassia Glauca L.*	*Caesalpiniaceae*	Leaf	Pseudosemiglabrin, (2S)-7,4'-dihydroxyflavan (4β→8)-catechin, (2S)-7,4'-dihydroxyflavan (4β→8)-gallocatechin	54
38.	*Clerodendron colebrkianum Walp.*	*Verbenaceae*	Leaf	Pilocarpine, glyceric acid, pangamic acid, gallic acid.	55
39.	*Cocculus hirsutus*	*Manispermaceae*	Whole plant	B-sitosterol, Trilobine, Isotrilobine, Syringaresionol, Protoquercitol, Ginnol and Glycosides	56
40.	*Cucurbita pepo L.*	*Cueurbitaceae*	Seed	Seed protein	57
41.	*Curcuma Longa L.*	*Zingiberaceae*	Rhizome	Curcumin	58
42.	*Ferula asafoetida*	*Apiaceae*	Oleo gum	Carvacrol, α-bisabolol	59
43.	*Glycyrrhizae radix*	*Leguminoceae*	Root	Liquiritigenin, Liquiritin, Isoliquiritigenin, Liquiritin apioside and Glycyrrhizin	60
44.	*Glycyrrhiza glabra*	*Papilionaceae*	root	Glycyrrhizin, Glycyrrhetinic acid	61

Some Herbal plants are used as hepatoprotective

To date, available modern drugs have not been able to come up with a satisfactory answer for liver disorders because of high costs and additional adverse effects. It is therefore necessary to search for alternative drugs for the treatment of liver diseases to replace the currently used drugs of doubtful efficacy and safety. There are numerous plants and polyherbal formulations claimed to have Hepatoprotective activity. Nearly phytoconstituents from 101 plants have been claimed to possess liver-protecting activity.[15] Thus there are some marketed products in India [Silybon (microlabs), LIV 52(Himalaya)] that are available as hepatoprotectives. At the same time surprisingly, we do not have readily available plant drugs/formulations to treat liver diseases. However, several medicinal plants have been advocated in traditional system of medicine, especially in Ayurveda, for treating liver disorders.[16]

Curcuma longa

Curcumin, often known as turmeric's yellow pigment, has anti-carcinogenic, anti-inflammatory, hepatoprotective, and antioxidant activities. Curcumin's liver-protective qualities are mostly related to its antioxidant capabilities. Curcumin consumption causes a decrease in liver structural changes and total bilirubin, as well as a drop in the activities of ALT, AST, ALP, LDH, GGT, and a rise in serum proteins. It demonstrated promising results in the treatment of cholestasis, hepatic fibrosis, and hepatic malignancies.[62]

Trigonella foenumgraecum

Trigonella foenumgraecum seeds have been shown to protect against hepatic diseases caused by ethanol, aluminum chloride, and diabetes. Irradiated rats were given 1g *Trigonella foenumgraecum* seed powder/kg body weight/day via gavage for 7 days before irradiation. *Trigonella foenumgraecum* therapy considerably reduced hepatic oxidative stress caused by radiation, as seen by considerable improvements in serum aminotransferase enzymes and ALP activity.[63]

Olea europaea

Olea europaea leaves contain maslinic acid, ursolic, oleanolic, quercetin, apigenin, luteolin, tannins, and caffeic acid Treatment of experimental animals with *Olea europaea* leaves extract caused a reduction in blood glucose prevention of hepatotoxicity.[64]

Figure 2: Herbal plants *(a) turmeric (b) Fenugreek (c) Olive*

Petroselinum crispum

Parsley leaves were used to cure colic, jaundice, constipation, flatulence, edema, and rheumatism. It was used to treat impotence, blood pressure regulation, lumbago, and nosebleeds. Chemical research has been conducted on the contents of parsley, which include ascorbic acid, carotenoids, flavonoids, coumarins, apiole, different terpenoid chemicals, phenylpropanoids, phthalides, furanocoumarins, and tocopherol. It is immunosuppressive, antioxidant, anti-diabetic, cytoprotective, and hepatoprotective.[63]

Caesalpinia crista

Caesalpinia crista is a Fabaceae family, genus of flowering plants in the legume family, also known as Karanja in Hindi, a large shrubby perennial climber found throughout India in the plains, wastelands, and coastal areas, up to an elevation of 1000 m in the hills. Saponins, flavonoids, alkaloids, and glycosides are among the bioactive chemicals found in *C. crista*.[65] This plant contains anti-inflammatory, antimalarial, anti-jaundice, anthelmintic, antidiabetic, antiperiodic, and antipyretic properties. Mishra et al. studied the hepatoprotective efficacy of ethanolic *C. crista* leaf extracts in PCM-induced hepatotoxicity in rats. Compared to the positive control group, the treatment with ethanolic extract (200 and 400 mg/kg) resulted in a significant decrease in higher levels of TB, serum marker enzymes, and TGA. Based on these findings, it was determined that ethanolic *C. crista* leaf extracts exhibited favorable hepatoprotective qualities in rats against PCM-induced liver damage.[66]

Cyathea gigantea

Cyathea gigantea is a tree fern that is usually distributed in the moist open areas of Thailand, Sri Lanka, Northeastern to Southern India, Western Java, and Nepal. This plant can grow up to 20 m have reported on the hepatoprotective effect of methanolic of *C. gigantean* leaf extract in PCM-induced toxicity in Wistar Albino rats. It was noted that the PCM intoxication led to histological and biochemical hepatic damage in the experimental rats.[67] On the other hand, the treatment with methanolic *C. gigantean* leaf extract decreased the elevated levels of ALP, serum glutamic oxaloacetic transaminase, TB, and serum glutamate-pyruvate transaminase; in addition, it also reversed the hepatic damage by restoring the structural integrity of the plasma membrane. The phytochemical screening showed that the leaf extract of *C. gigantean* comprises flavonoids, triterpenes, phenols, sterols, and saponins. These bioactive compounds might be responsible for its hepatoprotective potential. The findings from this study revealed the hepatoprotective potential of *C. gigantean* in PCM-induced-hepatotoxicity model in rats.[66]

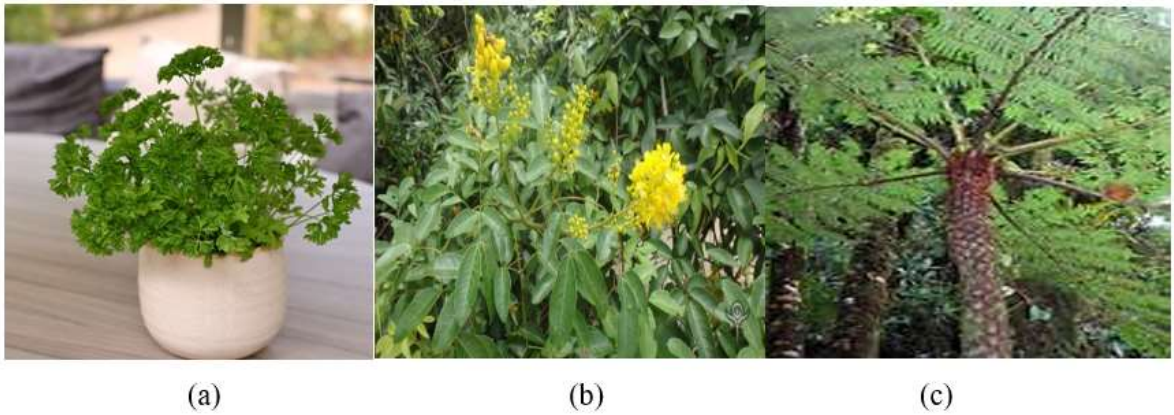

Figure 3: Herbal plants *(a) Parsley (b) Caesalpinia crista (c) Cyathea gigantea*

Aquilaria agallocha

This is a big tree growing up to 60–80 feet with thick a stem of 3–4 feet in diameter. It is native to Southeast Asia. The bark is papery thin and was sometimes used for writing just like Betula utilizing tree bark. Leaves are thin-like leather, shiny, and up to 3-inches long. Flowers are white and fruit is 1–2 inches long, smooth, and thin.[68] The plant *Aquilaria agallocha* has several pharmacological effects and shows anticancer, antioxidant, anti-inflammatory, antidiabetic, analgesic,

antihistaminic, antipyretic, laxative, antidiarrheal, antidiabetic, antihistaminic, anxiolytic, antimicrobial, sedative, antibacterial, ulcer, and anticonvulsant protective activities. Alam proved the hepatoprotective role of ethanolic extract of *A. agallocha* (AAE) leaves (400 mg/ml) in PCM-induced hepatotoxicity in Sprague–Dawley (SD) rats. These results revealed that AAE leaves exert a hepatoprotective effect as they exhibited a protective effect contrary to PCM-induced hepatotoxicity in SD rats as shown by a substantial decrease in AST, ALP, ALT, LDH, CHL, and TB, increase in ALB and total protein concentration, and prevention of PCM-induced histopathological changes in the liver.[66]

Flacourtia indica

The extracts of the aerial parts of *Flacourtia indica* (Burm. f.) Merr. were evaluated for hepato-protective properties. In paracetamol-induced hepatic necrosis in rat models, all extracts were found to reduce serum aspartate transaminase (AST), serum alanine transaminase (ALT), and serum alkaline phosphatase (ALP).[69] The most significant reduction of the serum level of AST and ALT was exhibited by petroleum ether and ethyl acetate extracts at a single oral dose of 1.5g/kg of body weight with a reduction of 29.0% AST & 24.0% ALT level by petroleum ether extract, and 10.57% AST & 6.7% ALT level by ethyl acetate extract compared to paracetamol (3 g/kg of body weight) treated animals. Histopathological examination also showed good recovery of paracetamol-induced necrosis by petroleum ether and ethyl acetate extracts.[70] On the other hand, the methanol extract did not show any remarkable effect on paracetamol-induced hepatic necrosis.[66] The hepatoprotective effects exhibited by petroleum ether and ethyl acetate extract might be mediated through the inhibition of microsomal drug-metabolizing enzymes. But, in this study the dose they have used is too high and it is not successful or rationale for human dose.[71]

Zingiber officinale

Ginger (*Zingiber officinale* Roscoe, Zingiberaceae) is widely used around the world in foods as a spice. For centuries, it has been an important ingredient in Chinese, Ayurvedic, and Tibb-Unani herbal medicines for the treatment of catarrh, rheumatism, nervous diseases, gingivitis, toothache, asthma, stroke, constipation, and diabetes Among the pharmacological effects demonstrated are anti-platelets, antioxidant, antitumor, anti-rhino viral, anti-hepatotoxicity, anti-arthritic and anti-inflammatory.[72] The antioxidant activity of gingerol and other constituents of ginger has been confirmed. Different doses of ginger extract cause alterations in biochemical parameters, free radicals, antioxidant enzymes, and drug-metabolizing enzymes induced by bromobenzene in the liver of male rats and alleviating the toxicity of bromobenzene in the liver. Curcumin, another active component present in ginger, was found to be an antioxidant and anti-inflammatory agent and induced haem oxygenase-1 and protected endothelial cells against oxidative stress.[73] The antioxidants inhibit the reactive oxygen species (ROS), which are capable of causing DNA damage, associated with carcinogenesis, coronary heart disease, and many other health problems related to advancing age. The aqueous extract of ginger root may cause hepatoprotective effects against aspartame, which may cause hepatotoxicity and oxidative stress.[74] Ginger root extract has hepatoprotective effect against aspartame-induced hepatotoxicity and decreased liver function markers (ALT, AST, ALP, γ-GT), serum total protein, albumin and total bilirubin levels, serum LDH activity, α-fetoprotein, and tumor necrosis factor (TNF), increased levels of antioxidant enzymes, and reduced levels of malondialdehyde.[75]

Figure 4: Herbal plants *(a) Aquilaria agallocha (b) Flacourtia indica (c) Zingiber officinale*

Cucurbita pepo L.

Pumpkin seeds (*Cucurbita pepo L.*) are a rich source of unsaturated fatty acids, antioxidants, and fibers, known to have anti-atherogenic and hepatoprotective activities. Pumpkin is one such plant that has been frequently used as functional food or medicine. Some of its common uses in most countries are for diabetes where it is used internally as well as externally for the management of worms and parasites. Treatment of spontaneously hypertensive rats with felodipine or captopril monotherapy or combined with pumpkin seed oil produced improvement in the measured free radical scavengers in the heart and kidney.[76] Pumpkin is also rich in unsaturated fatty acids especially linoleic and oleic acid and tocopherols and with very high oxidative stability. In addition to the carotenoids and gamma-aminobutyric acids (GABA) found in the fruits, there are other biologically active ingredients, which are found in pumpkins, such as sterols, proteins, peptides, polysaccharides, para-aminobenzoic acid, and fixed oils.[77] Pumpkin seed oil's main nutrients are essential fatty acid-omega 6, omega 9, phytosterols, and antioxidants such as carotenoids, vitamin A, and vitamin E. Linoleic acid, a polyunsaturated fatty acid present in pumpkin seed oil, is known to increase membrane fluidity and allows for osmosis, intracellular and extracellular gaseous exchange.[78] Pumpkin seed oil includes fatty acids: palmitic (C 16:0), stearic (C 18:0), oleic (C 18:1), and linoleic (C 18:2). Antioxidants are the substances that when present in low

concentration significantly delay or reduce the oxidation of the substrate. Pumpkin oil may play an important role in the protection against alcohol-induced hepatotoxicity and oxidative stress.[79] Pretreatment with pumpkin oil may have hepatoprotective effects, which are varied and include oxidation, anti-lipid peroxidation enhanced detoxification, and protection against glutathione depletion.[80]

Andrographis paniculata

Andrographis paniculata (A. paniculata), known among the Indians, is one of the most commonly used plants in the traditional systems of Unani and Ayurvedic medicines. It is called Creat in English and is known as the king of bitters. The aerial parts are most commonly used; however, the whole plant or the roots are also used for certain purposes in some manuscripts.[81] *A. paniculata* has been reported as having antibacterial, anti-malarial, antiviral, cardioprotective, antioxidant, anti-inflammatory, antidiabetic effects and also antitumor activities.[82] Treatment with whole plant extract of *A. paniculata* effectively reduced the level of lipid peroxidation and increased the status of antioxidant enzymes. This may be due to the presence of various flavonoids, phenols, and glycosides in the drug.[83]

Allium sativum

Allium sativum contains fatty acids, proteins, carbohydrates, fiber, glycolipids, phospholipids, glycosides lectins, saponins, ajoene, allicin, diallyl trisulfide, diallyl disulfide, SAC sulfoxide, B, E, and C vitamins, which may be responsible for protection from various disorders and tissue damage.[84] Aged *Allium sativum* extract has a high antioxidant content. However, free radical scavenging activity has been suggested as a possible mechanism of hepatoprotective action.[85,86]

Figure 5: Herbal plants *(a) Cucurbita pepo L. (b) Andrographis paniculata (c) Allium sativum*

Conclusion

Herbal medications have the potential to be an effective treatment for liver problems. An extensive review of the literature on hepatoprotective plants clearly shows that herbal medications have significant promise for the treatment of liver ailments. We also presented the available data in the literature for different plants' phytochemical elements. As a result, we conclude that herbs are an important source of hepatoprotective and liver regeneration drugs. More study is needed, however, to identify, characterize, and standardize the active substances, beneficial compounds, and formulations for the treatment of liver illnesses. The availability of modern hepatoprotective medications with realistic clinical utility is still quite restricted, and the discovery of new compounds with similar potentials will undoubtedly encourage the drug discovery process.

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References

1. Asif A, Park SH, Soomro AM, Khalid MAU, Salih ARC, Kang B, et al. Microphysiological system with continuous analysis of albumin for hepatotoxicity modeling and drug screening. J Ind Eng Chem. 2021; 98:318-26. https://doi.org/10.1016/j.jiec.2021.03.035

2. Thyagarajan SP, Jayaram S, Gopalakrishnan V, Hari R, Jeyakumar P, Sripathi MS. Herbal medicines for liver diseases in India. J Gastroenterol Hepatol. 2002; 17:S370-6. https://doi.org/10.1046/j.1440-1746.17.s3.30.x PMid:12472966

3. Hayes SC, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and commitment therapy: Model, processes and outcomes. Behav Res Ther. 2006; 44(1):1-25. https://doi.org/10.1016/j.brat.2005.06.006 PMid:16300724

4. Bischoff K, Mukai M, Ramaiah SK. Liver toxicity. In: Veterinary toxicology. Elsevier; 2018. p. 239-57. https://doi.org/10.1016/B978-0-12-811410-0.00015-5 PMid:30392128

5. Iqubal A, Iqubal MK, Haque SE. Experimental hepatotoxicity inducing agents: a Review. Int J Clin Pharmacol Res. 2016; 6(11):325-35.

6. Gao B. Hepatoprotective and anti-inflammatory cytokines in alcoholic liver disease. J Gastroenterol Hepatol. 2012; 27:89-93. https://doi.org/10.1111/j.1440-1746.2011.07003.x PMid:22320924 PMCid:PMC3281557

7. Pandit A, Sachdeva T, Bafna P. Drug-induced hepatotoxicity: a review. J Appl Pharm Sci. 2012; (Issue):233-43. https://doi.org/10.7324/JAPS.2012.2541

8. Butt F, Shahid M, Hassan M, Tawakkal F, Amin I, Afzal S, et al. A review on hepatitis C virus: role of viral and host-cellular factors in replication and existing therapeutic strategies. Egypt Liver J. 2022; 12(1):1-8. https://doi.org/10.1186/s43066-022-00232-w

9. Mayuren C, Reddy VV, Priya SV, Devi VA. Protective effect of Livactine against CCl4 and paracetamol induced hepatotoxicity in adult Wistar rats. N Am J Med Sci. 2010; 2(10):491. https://doi.org/10.4297/najms.2010.2491 PMid:22558553 PMCid:PMC3339113

10. Ilyas U, Katare DP, Aeri V, Naseef PP. A review on hepatoprotective and immunomodulatory herbal plants. Pharmacogn Rev. 2016; 10(19):66. https://doi.org/10.4103/0973-7847.176544 PMid:27041876 PMCid:PMC4791991

11. Madrigal-Santillán E, Madrigal-Bujaidar E, Álvarez-González I, Sumaya-Martínez MT, Gutiérrez-Salinas J, Bautista M, et al. Review of natural products with hepatoprotective effects. World J

Gastroenterol WJG. 2014; 20(40):14787. https://doi.org/10.3748/wjg.v20.i40.14787 PMid:25356040 PMCid:PMC4209543

12. Rouf R, Ghosh P, Uzzaman MR, Sarker DK, Zahura FT, Uddin SJ, et al. Hepatoprotective plants from Bangladesh: a biophytochemical review and future prospect. Evidence-based Complement Altern Med. 2021; 2021. https://doi.org/10.1155/2021/1633231 PMid:34504532 PMCid:PMC8423546

13. Tabeshpour J, Hosseinzadeh H, Hashemzaei M, Karimi G. A review of the hepatoprotective effects of hesperidin, a flavanon glycoside in citrus fruits, against natural and chemical toxicities. DARU J Pharm Sci. 2020; 28:305-17. https://doi.org/10.1007/s40199-020-00344-x PMid:32277430 PMCid:PMC7214587

14. Saleem TSM, Chetty CM, Ramkanth S, Rajan VST, Kumar KM, Gauthaman K. Hepatoprotective herbs-a review. Int J Res Pharm Sci. 2010; 1(1):1-5.

15. Ali SA, Sharief NH, Mohamed YS. Hepatoprotective activity of some medicinal plants in Sudan. Evidence-Based Complement Altern Med. 2019; 2019. https://doi.org/10.1155/2019/2196315 PMid:31929810 PMCid:PMC6935815

16. Srivastava R, Srivastava P. Hepatotoxicity and the role of some herbal hepatoprotective plants in present scenario. GJ Dig Dis. 2018; 3(2):2. https://doi.org/10.4172/2472-1891.100034

17. Thagriki DS, Ray U. An overview of traditional medicinal plants as dengue virus inhibitors. Trends Phytochem Res. 2022; 6(2):116-36.

18. Xu Z, Wang C, Luan Z, Zhang D, Dong B. Exploring the potential targets of the Abrus cantoniensis Hance in the treatment of hepatitis E based on network pharmacology. Front Vet Sci. 2023; 10:1155677. https://doi.org/10.3389/fvets.2023.1155677 PMid:37035802 PMCid:PMC10076809

19. Sharma S, Sahu AN. Development, characterization, and evaluation of hepatoprotective effect of Abutilon indicum and Piper longum phytosomes. Pharmacognosy Res. 2016; 8(1):29. https://doi.org/10.4103/0974-8490.171102 PMid:26941533 PMCid:PMC4753757

20. Jayasekhar P, Mohanan P V, Rathinam K. Hepatoprotective activity of ethyl acetate extract of Acacia catechu. Indian J Pharmacol. 1997; 29(6):426.

21. Faujdar S, Sati B, Sharma S, Pathak AK, Paliwal SK. Phytochemical evaluation and anti-hemorrhoidal activity of bark of Acacia ferruginea DC. J Tradit Complement Med. 2019; 9(2):85-9. https://doi.org/10.1016/j.jtcme.2018.02.003 PMid:30963042 PMCid:PMC6435949

22. Akare S, Sahare A, Shende M, Bondre A, Wanjari A. Hepatoprotective activity of Acacia Ferruginea DC. Leaves against carbon tetrachloride induced liver damage in rats. Int J PharmTech Res. 2009; 1(3):962-5.

23. Yaeesh S, Jamal Q, Khan A, Gilani AH. Studies on hepatoprotective, antispasmodic and calcium antagonist activities of the aqueous-methanol extract of Achillea millefolium. Phyther Res An Int J Devoted to Pharmacol Toxicol Eval Nat Prod Deriv. 2006; 20(7):546-51. https://doi.org/10.1002/ptr.1897 PMid:16619341

24. Fahim NF, Sathi ZS. Assesment of hepatoprotective activity of roots and barks of Achyranthes aspera in carbon tetrachloride-induced hepatotoxicity in rats. Malays J Halal Res. 2018; 1(2):23-6. https://doi.org/10.26480/mjhr.02.2018.23.26

25. Singanan V, Singanan M, Begum H. The hepatoprotective effect of bael leaves (Aegle marmelos) in alcohol induced liver injury in albino rats. Int J Sci Technol. 2007; 2(2):83-92.

26. Chandan BK, Saxena AK, Shukla S, Sharma N, Gupta DK, Suri KA, et al. Hepatoprotective potential of Aloe barbadensis Mill. against carbon tetrachloride induced hepatotoxicity. J Ethnopharmacol. 2007; 111(3):560-6. https://doi.org/10.1016/j.jep.2007.01.008 PMid:17291700

27. Harmayani E, Anal AK, Wichienchot S, Bhat R, Gardjito M, Santoso U, et al. Healthy food traditions of Asia: exploratory case studies from Indonesia, Thailand, Malaysia, and Nepal. J Ethn Foods. 2019; 6:1-18. https://doi.org/10.1186/s42779-019-0002-x

28. Nagalekshmi R, Menon A, Chandrasekharan DK, Nair CKK. Hepatoprotective activity of Andrographis paniculata and Swertia chirayita. Food Chem Toxicol. 2011; 49(12):3367-73. https://doi.org/10.1016/j.fct.2011.09.026 PMid:21983487

29. Shaikh S, Dubey R, Dhande S, Joshi YM, Kadam VJ. Phytochemical and pharmacological profile of Aphanamixis polystachya: an overview. Res J Pharm Technol. 2012; 5(10):1260-3.

30. Shivashri C, Rajarajeshwari T, Rajasekar P. Hepatoprotective action of celery (Apium graveolens) leaves in acetaminophen-fed freshwater fish (Pangasius sutchi). Fish Physiol Biochem. 2013; 39:1057-69. https://doi.org/10.1007/s10695-012-9762-6 PMid:23288624

31. Alam A, Khan AA. Argemone mexicana L.: A weed with versatile medicinal and pharmacological applications. Ann Phytomedicine Int J. 2020; 9(1):218-23. https://doi.org/10.21276/ap.2020.9.1.29

32. Chauhan NS, Dixit VK. Asteracantha longifolia (L.) Nees, Acanthaceae: chemistry, traditional, medicinal uses and its pharmacological activities-a review. Rev Bras Farmacogn. 2010; 20:812-7. https://doi.org/10.1590/S0102-695X2010005000022

33. Kanase V, Mane DJ. A pharmacognostic and pharmacological review on Alstonia scholaris. Asian J Pharm Clin Res. 2018; 11(12):22-6. https://doi.org/10.22159/ajpcr.2018.v11i12.28124

34. Lu Q, Gu W, Luo C, Wang L, Hua W, Sun Y, et al. Phytochemical characterization and hepatoprotective effect of active fragment from Adhatoda vasica Nees. against tert-butyl hydroperoxide induced oxidative impairment via activating AMPK/p62/Nrf2 pathway. J Ethnopharmacol. 2021; 266:113454. https://doi.org/10.1016/j.jep.2020.113454 PMid:33065254

35. Zahid M, Arif M, Rahman MA, Mujahid M. Hepatoprotective and antioxidant activities of Annona squamosa seed extract against alcohol-induced liver injury in Sprague Dawley rats. Drug Chem Toxicol. 2020; 43(6):588-94. https://doi.org/10.1080/01480545.2018.1517772 PMid:30239227

36. Abidullah S, Rauf A, Khan SW, Ayaz A, Liaquat F, Saqib S. A comprehensive review on distribution, paharmacological uses and biological activities of Argyrolobium roseum (Cambess.) Jaub. & Spach. Acta Ecol Sin. 2022; 42(3):198-205. https://doi.org/10.1016/j.chnaes.2021.03.009

37. Vallès J, Garcia S, Hidalgo O, Martín J, Pellicer J, Sanz M, et al. Biology, genome evolution, biotechnological issues and research including applied perspectives in Artemisia (Asteraceae). Adv Bot Res. 2011; 60:349-419. https://doi.org/10.1016/B978-0-12-385851-1.00015-9

38. D'Aria F, Pagano B, Giancola C. Thermodynamic properties of hydroxypropyl-β-cyclodextrin/guest interaction: a survey of recent studies. J Therm Anal Calorim. 2022; 147(8):4889-97. https://doi.org/10.1007/s10973-021-10958-1

39. Sani I, Umar RA, Hassan SW, Faruq UZ, Bello F, Aminu H, et al. Hepatoprotective effect of Azadirachta indica leaf fractionated extracts against snake venom toxicity on albino rats. Saudi J Biomed Res. 2020; 5(6):112-7. https://doi.org/10.36348/sjbr.2020.v05i06.004

40. Murthy HN, Yadav GG, Dewir YH, Ibrahim A. Phytochemicals and biological activity of desert date (Balanites aegyptiaca (L.) Delile). Plants. 2020; 10(1):32. https://doi.org/10.3390/plants10010032 PMid:33375570 PMCid:PMC7823407

41. Minnady M, Jayapal G, Poochi S, Nethaji P, Mathalaimuthu B. Hepatoprotective Effect of Indigenous Medicinal Plants-A Review. Indian J Pharm Sci. 2022; 84(5):1116-32. https://doi.org/10.36468/pharmaceutical-sciences.1006

42. Kumar GVS. An emphasis on global use of traditional medicinal system and herbal hepatoprotective drugs. J Pharm Res. 2014; 8:28-37.

43. Gul H, Awais M, Saddick S, Ahmed Y, Khan FS, Ahmed E, et al. Quantification of biochemical compounds in Bauhinia Variegata Linn flower extract and its hepatoprotective effect. Saudi J Biol Sci. 2021; 28(1):247-54 https://doi.org/10.1016/j.sjbs.2020.09.056 PMid:33424304 PMCid:PMC7785441

44. Venmathi Maran BA, Iqbal M, Gangadaran P, Ahn BC, Rao PV, Shah MD. Hepatoprotective potential of Malaysian medicinal plants: a review on phytochemicals, oxidative stress, and antioxidant mechanisms. Molecules. 2022; 27(5):1533. https://doi.org/10.3390/molecules27051533 PMid:35268634 PMCid:PMC8911738

45. Paudel K, Ramamurthy A, Sharma G. Some important hepatoprotective medicinal plants in Ayurveda-a review. Int J Ayurveda Res. 2020; 3(8):138-50. https://doi.org/10.47223/IRJAY.2020.3815

46. Anjum N, Ridwan Q, Akhter F, Hanief M. Phytochemistry and therapeutic potential of Berberis lycium Royle; an endangered species of Himalayan region. Acta Ecol Sin. 2022; https://doi.org/10.1016/j.chnaes.2022.09.005

47. Thajudeen KY, Alsayari A, Najib Ullah SNM, Salam S, Elayadeth-Meethal M, Uoorakkottil I. Validation, Optimization and Hepatoprotective Effects of Boeravinone B and Caffeic Acid Compounds from Boerhavia diffusa Linn. Separations. 2022; 9(7):177. https://doi.org/10.3390/separations9070177

48. Latif A, Ashiq K, Qayyum M, Ashiq S, Ali E, Anwer I. PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE OF THE MEDICINAL HERB: BRYOPHYLLUM PINNATUM. JAPS J Anim Plant Sci. 2019; 29(6).

49. Konno T, Ninomiya K, Yoshikawa M, Matsuda H, Morikawa T. Triterpene saponin constituents from roots of Bupleurum falcatum: Hepatoprotective effects on D-galactosamine-induced cell damage. Planta Med. 2016; 82(S 01):P478. https://doi.org/10.1055/s-0036-1596563

50. Kaur V, Kumar M, Kaur P, Kaur S, Singh AP, Kaur S. Hepatoprotective activity of Butea monosperma bark against thioacetamide-induced liver injury in rats. Biomed Pharmacother. 2017; 89:332-41. https://doi.org/10.1016/j.biopha.2017.01.165 PMid:28237915

51. Kalantari H, Foruozandeh H, Khodayar MJ, Siahpoosh A, Saki N, Kheradmand P. Antioxidant and hepatoprotective effects of Capparis spinosa L. fractions and Quercetin on tert-butyl hydroperoxide-induced acute liver damage in mice. J Tradit Complement Med. 2018; 8(1):120-7. https://doi.org/10.1016/j.jtcme.2017.04.010 PMid:29321999 PMCid:PMC5755993

52. Mwangi RW, Macharia JM, Wagara IN, Bence RL. The medicinal properties of Cassia fistula L: A review. Biomed Pharmacother. 2021; 144:112240. https://doi.org/10.1016/j.biopha.2021.112240 PMid:34601194

53. Qayoom I, Ansari AP, Huzaifa A, Habib A, Reshi BM, Ahmed NZ, et al. San'(Cassia angustifolia Vahl.): A Potent Detoxifying Drug in Unani System of Medicine-An Appraisal/Insight. 2022;

54. Farswan M, Mazumder PM, Percha V. Protective effect of Cassia glauca Linn. on the serum glucose and hepatic enzymes level in streptozotocin induced NIDDM in rats. Indian J Pharmacol. 2009; 41(1):19. https://doi.org/10.4103/0253-7613.48887 PMid:20177576 PMCid:PMC2825008

55. Das RJ, Pathak K, Bordoloi S, Saikia R, Alqahtani SA, Saharia J, et al. Clerodendrum colebrookianum Walp: An Insight into its Pharmacology, Expository Traditional Uses and Extensive Phytochemistry. Curr Tradit Med. 2023; 9(2):56-63. https://doi.org/10.2174/2215083808666220623112606

56. Djahra AB, Lmhanat I, Benkaddour M, Benkherara S, Laib I, Benine C. Traditional Herbal Remedies from Algeria for Treating Digestive Disorders. J Drug Deliv Ther. 2023; 13(1):84-92. https://doi.org/10.22270/jddt.v13i1.5906

57. El-Hadary A. Comparison of the Chemical Compositions, Physiochemical Analysis and Other Bioactive Compounds of Various Pumpkin (curcubita pepo l.) Varieties. Ann Agric Sci Moshtohor. 2023; 61(1):69-76.

58. Aprioku JS, Amamina AM, Nnabuenyi PA. Mancozeb-induced hepatotoxicity: protective role of curcumin in rat animal model. Toxicol Res (Camb). 2023; 12(1):107-16. https://doi.org/10.1093/toxres/tfac085 PMid:36866214

59. Mahmoud AM, Alruhaimi RS, Hassanein EHM. Ferula asafoetida. In: Herbs, Spices and their Roles in Nutraceuticals and Functional Foods. Elsevier; 2023. p. 233-43. https://doi.org/10.1016/B978-0-323-90794-1.00020-X

60. Huo X, Gu Y, Zhang Y. The discovery of multi-target compounds with anti-inflammation activity from traditional Chinese medicine by TCM-target effects relationship spectrum. J Ethnopharmacol. 2022; 293:115289. https://doi.org/10.1016/j.jep.2022.115289 PMid:35427724

61. Esmaeili H, Karami A. Phytochemical, Pharmacological, and Health Benefits of Glycyrrhiza glabra. Handb Nutraceuticals Nat Prod Biol Med Nutr Prop Appl. 2022; 2:361-81. https://doi.org/10.1002/9781119746843.ch28

62. Khan H, Ullah H, Nabavi SM. Mechanistic insights of hepatoprotective effects of curcumin: Therapeutic updates and future prospects. Food Chem Toxicol. 2019; 124:182-91. https://doi.org/10.1016/j.fct.2018.12.002 PMid:30529260

63. Patel N, Patel MK. Medicinal plants with hepatoprotective potential: A brief review.

64. Almatroodi SA, Almatroudi A, Anwar S, Yousif Babiker A, Khan AA, Alsahli MA, et al. Antioxidant, anti-inflammatory and hepatoprotective effects of olive fruit pulp extract: in vivo and in vitro study. J Taibah Univ Sci. 2020; 14(1):1660-70. https://doi.org/10.1080/16583655.2020.1848761

65. Chan EWC, Tangah J, Baba S, Chan HT, Kainuma M, Inoue T. Caesalpinia crista: A coastal woody climber with promising therapeutic values. J Appl Pharm Sci. 2018; 8(3):133-40.

66. Okaiyeto K, Nwodo U, Mabinya L, Okoh A. A review on some medicinal plants with hepatoprotective effects. Pharmacogn Rev. 2018; 12(24):186-99. https://doi.org/10.4103/phrev.phrev_52_17

67. Marimuthu alias Antonysamy J, George V, Iruthayamani SJ, Balasundaram S. Bioactive Compounds and Biological Activities of Cyathea Species. Bioact Compd Bryophyt Pteridophytes. 2023; 471-90. https://doi.org/10.1007/978-3-031-23243-5_17

68. Alam J, Mujahid M, Rahman MA, Akhtar J, Khalid M, Jahan Y, et al. An insight of pharmacognostic study and phytopharmacology of Aquilaria agallocha. J Appl Pharm Sci. 2015; 5(8):173-81. https://doi.org/10.7324/JAPS.2015.50827

69. Kumar A. A review on hepatoprotective herbal drugs. Int J Res Pharm Chem. 2012; 2(1):96-102.

70. Nazneen M, Mazid MA, Kundu JK, Bachar SC, Begum F, Datta BK. Protective effects of Flacourtia indica aerial parts extracts against paracetamol-induced hepatotoxiciy in rats. J taibah Univ Sci. 2009; 2:1-6. https://doi.org/10.1016/S1658-3655(12)60001-6

71. Pai A, Shenoy C. Hepatoprotective activity of Flacourtia jangomas (Lour.) Raeuschleaves and fruit methanolic extract on paracetamol-induced hepatotoxicity in HepG2 Cells. Biomedicine. 2021; 41(3):587-91. https://doi.org/10.51248/.v41i3.1197

72. Huang YS. The hepatoprotective effect of ginger. J Chinese Med Assoc. 2019; 82(11):805-6. https://doi.org/10.1097/JCMA.0000000000000174 PMid:31693531

73. Abdel-Azeem AS, Hegazy AM, Ibrahim KS, Farrag ARH, El-Sayed EM. Hepatoprotective, antioxidant, and ameliorative effects of ginger (Zingiber officinale Roscoe) and vitamin E in acetaminophen treated rats. J Diet Suppl. 2013; 10(3):195-209. https://doi.org/10.3109/19390211.2013.822450 PMid:23927622

74. Akinloye OA, Somade OT, Akindele AS, Adelabu KB, Elijah FT, Adewumi OJ. Anticlastogenic and hepatoprotective properties of ginger (Zingiber officinale) extract against nitrobenzene-induced toxicity in rats. Rom J Biochem. 2014; 51(1):3-15.

75. Fahmi A, Hassanen N, Abdur-Rahman M, Shams-Eldin E. Phytochemicals, antioxidant activity and hepatoprotective effect of ginger (Zingiber officinale) on diethylnitrosamine toxicity in rats. Biomarkers. 2019; 24(5):436-47. https://doi.org/10.1080/1354750X.2019.1606280 PMid:30979347

76. Ratnam N, Naijibullah M, Ibrahim MD. A review on Cucurbita pepo. Int J Pharm Phytochem Res. 2017; 9:1190-4. https://doi.org/10.25258/phyto.v9i09.10305

77. Abou Seif HS. Ameliorative effect of pumpkin oil (Cucurbita pepo L.) against alcohol-induced hepatotoxicity and oxidative stress in albino rats. Beni-suef Univ J basic Appl Sci. 2014; 3(3):178-85. https://doi.org/10.1016/j.bjbas.2014.08.001

78. Radić I, Mirić M, Mijović M, Tatalović N, Mitić M, Nestorović V, et al. Protective effects of pumpkin (Cucurbita pepo L.) seed oil on rat liver damage induced by chronic alcohol consumption. Arch Biol Sci. 2021; 73(1):123-33. https://doi.org/10.2298/ABS201205008R

79. Elmeligy MH, Farid AS, Fararh K. Antioxidant and hepatoprotective effect of pumpkin seed oil in CCl4-intoxicated rats. Benha Vet Med J. 2019; 36(2):77-89. https://doi.org/10.21608/bvmj.2019.13448.1030

80. Adepoju GKA, Adebanjo AA. Effect of consumption of Cucurbita pepo seeds on haematological and biochemical parameters. African J Pharm Pharmacol. 2011; 5(1):18-22. https://doi.org/10.5897/AJPP10.186

81. Nyeem MA Bin, Mannan MA, Nuruzzaman M, Kamrujjaman KM, Das SK. Indigenous king of bitter (Andrographis paniculata): A review. J Med Plants Stud. 2017; 5(2):318-24.

82. Mehta S, Sharma AK, Singh RK. Therapeutic journey of Andrographis paniculata (Burm. f.) Nees from natural to synthetic and nanoformulations. Mini Rev Med Chem. 2021; 21(12):1556-77. https://doi.org/10.2174/1389557521666210315162354 PMid:33719961

83. Jain K, Majee C. Hepatoprotective activity of andrographolide and its semi-synthetic derivatives. Res J Pharm Technol. 2022; 15(9):4055-60. https://doi.org/10.52711/0974-360X.2022.00680

84. Guan MJ, Zhao N, Xie KQ, Zeng T. Hepatoprotective effects of garlic against ethanol-induced liver injury: A mini-review. Food Chem Toxicol. 2018; 111:467-73. https://doi.org/10.1016/j.fct.2017.11.059 PMid:29208504

85. Azab AE, Albasha MO. Hepatoprotective effect of some medicinal plants and herbs against hepatic disorders induced by hepatotoxic agents. J Biotechnol Bioeng. 2018; 2(1):8-23.

86. Mustafa MA, Helal EGE, El Sayed RAA, Ebrahiem S. Effect of trigonella, allium sativum and their mixture on some physiological parameters in hyperthyroidimic rats. Egypt J Hosp Med. 2018; 71(4):3049-55.