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Hepatitis and medicinal plants: An overview

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Abstract
The Liver is a vital organ of paramount importance involved in the maintenance of metabolic functions and detoxification of the exogenous and endogenous challenges like xenobiotic, drugs, viral infections and chronic alcoholism. Liver diseases are a major worldwide health problem, with high endemicity in developing countries. They are mainly caused by chemicals and some drugs when taken in very high doses. Despite advances in modern medicine, there is no effective drug available that stimulates liver function, offer protection to the liver from damage or help to regenerate hepatic cells. There is urgent need, therefore, for effective drugs to replace supplement those in current use. The plant kingdom is undoubtedly valuable as a source of new medicinal agents. Herbal remedies are focused in the pharmaceutical industry to evolve a safe route for liver disorders. There is no plant in this Universe which is non-medicinal and which cannot be made of use for many purposes and by many modes. This definition rightly suggests that in principle all plants have a potential medicinal value. Medicinal plants have been considered as important therapeutic aid for alleviating ailment of humankind. Search for eternal health and longevity and to seek remedy to relieve pain and discomfort prompted the early man to explore his immediate natural surroundings to develop a variety of therapeutic agents using natural resources.
Liver cell injury caused by various toxic chemicals (certain anti-biotic, chemotherapeutic agents, carbon tetrachloride (CCL_4), thioacetamide (TAA) etc., excessive alcohol consumption and microbes is well-studied. Herbal medicines have been used in the treatment of liver diseases for a long time. A number of herbal preparations are available in the market.
The focus of this review is to elucidate the importance of liver and aimed at compiling data based on reported works on medicinal plants that have been tested in hepato-toxicity models and proved as hepato-protective.

Keywords: Hepatitis, medicinal plants, pharmaceutical industry

Introduction
Liver is the largest glandular organ in the body which works all the time to keep the body healthy. The liver is important because a person's nutritional level is not only determined by what he or she eats, but by what the liver processes. The incredible complexity of liver chemistry and its fundamental role in human physiology is so daunting to researchers that the thought that simple plant remedies might have something to offer is astonishing and incredible!
Liver is considered to be one of the most vital organs that functions as a Centre of metabolism of nutrients such as carbohydrates, proteins and lipids and excretion of waste metabolites. Additionally, it is also handling the metabolism and excretion of drugs and other xenobiotic from the body thereby providing protection against foreign substances by detoxifying and eliminating them. It is involved with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction. The bile secreted by the liver has, among other things, plays an important role in digestion. Therefore, maintenance of a healthy liver is essential for the overall well-being of an individual. Liver cell injury caused by various toxicants such as certain chemotherapeutic agents, carbon tetrachloride, thioacetamide, chronic alcohol consumption and microbes are common.
Enhanced lipid per oxidation during metabolism of ethanol may result in development of hepatitis leading to cirrhosis. Herbal drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness. The Indian Traditional Medicine like Ayurveda, Siddha and Unani are predominantly based on the use of plant materials. The association of medical plants with other plants in their habitat also influences their medicinal values in some cases. One of the important and well documented uses of plant products is their use as hepatoprotective agents.
Hence, there is an ever increasing need for safe hepatoprotective agent. In spite of tremendous strides in modern medicine, there are hardly any drugs that stimulate liver function, offer

protection to the liver from damage or help regeneration of hepatic cell. Many formulations containing herbal extracts are sold in the Indian market for liver disorders but management of liver disorders by a simple and precise herbal drug is still an intriguing problem. Several Indian medicinal plants have been extensively used in the Indian traditional system of medicine for the management of liver disorder. Some of these plants have already been reported to posse's strong antioxidant activity.

It is estimated that about 7,500 plants are used in local health traditions in, mostly, rural and tribal villages of India. Out of these, the real medicinal value of over 4,000 plants is either little known or hitherto unknown to the main stream population. The classical systems of medicine such as Ayurveda, Siddha, Amchi, Unani and Tibetan use about 1,200 plants. A detailed investigation and documentation of plants used in local health traditions and pharmacological evaluation of these plants and their taxonomical relatives can lead to the development of invaluable plant drugs for many dreaded diseases. Liver cell injury caused by various toxic chemicals like certain-antibiotic, chemotherapeutic agents, carbon tetrachloride (CCl4), thioacetamide (TAA) etc. excessive alcohol consumption and microbes is well studied. The available synthetic drugs to treat liver disorders in this condition also cause further damage to the liver.

Hence, Herbal drugs have become increasingly popular and their use is widespread. Herbal medicines have been used in the treatment of liver diseases for a long time. A number of herbal preparations are available in the market. The present review is aimed at compiling data on promising phytochemicals from medicinal plants that have been tested in hepatotoxicity models using modern scientific system.

Medicinal plants play a key role in the human health care. About 80% of the world population relies on the use of traditional medicine which is predominantly based on plant materials. The present review is aimed at compiling data based on reported works

On promising phytochemicals and pharmacological activities from medicinal plants that have been tested for their hepatoprotective activity.

Causes of Liver Diseases

Though the liver is effective in the detoxification of foreign bodies, with its numerous but vital activities, the liver becomes a target organ for diseases, and is pre-disposed it to a high risk of liver diseases, causing hepatitis (a condition characterized by the destruction of liver cells and the inflammation of cells in the liver tissues), and subsequently, jaundice.

There are various causes of liver diseases, generally resulting from viral or protozoal infections, excessive use of alcohol, drugs and xenobiotic.

Acute hepatitis may be caused by

- Viral infections such as hepatitis A, hepatitis B, hepatitis C, hepatitis D and hepatitis E, and other viral diseases such as mononucleosis caused by cytomegalovirus, Severe bacterial infections, Amoebic infections,
- Increasing intake of medicines, e.g. acetaminophen (which can be hepatotoxic) and halothane (an anesthetic) Poisoning from intake of alcohol, and fungal toxins, like toadstool poisoning.
- Chronic hepatitis is mainly caused by: Contagious viral infections such as hepatitis B, hepatitis C and hepatitis D,
- Hepatotoxic medicines such as isoniazid (INH) (anti-tuberculosis), methyldopa (Aldomet) adrenergic antihypertensive and tetracycline (an antibiotic), High alcohol intake,
- Inborn metabolic disorders, such as Wilson's disease (disorder of the body's copper metabolism) and haemochromatosis (disorder of the body's iron metabolism),
- Liver cancer, Cirrhosis of the liver, Incidence of the various disease conditions and its associated risks are high, and is therefore a major health problem.

Epidemiology of Liver Diseases

Primarily, liver diseases with hepatitis compromises the storage and synthesis of glucose, affecting CNS function and mental processing, causes fatigue and general ailment and unwell being. It also disrupts storage and use of calories, causing fatigue and body mass wasting.

Since the liver is primarily responsible for amino acid metabolism and nitrogen removal from body, a diseased liver causes a decrease in glucose synthesis, affecting CNS function and causing fatigue; also causes accumulation of nitrogen waste with immense toxic effect on many tissues.

Additionally, effective water distribution is not maintained, causing edema. There is also general alteration in cell function, causing general malaise and fatigue. Disease of the liver also causes malfunction in circulation, detrimental to survival.

Another major consequence of liver damage is a loss in the body's ability to detoxify and eliminate foreign substances, causing general toxicity and general malaise. Of the known hepatitis viruses, three can cause persistent infection and chronic hepatitis: the hepatitis B virus (HBV), the hepatitis C virus (HCV) and the hepatitis delta (or hepatitis D) virus (HDV) Hepatitis A and E cause acute, self-limited disease only.

Aside the effects hepatitis has on the liver, it also has an adverse effect on other vital organs such as the heart, with no known link. The combined infection of human cytomegalic virus and hepatitis C virus is reported to increase the risk of allograft vascular disease in heart transplant recipient's shows that HCV sero-positivity is found to be associated with inflammatory markers and heart failure events in persons with coronary heart disease. Though vaccination for Hepatitis has been resorted to and its long-term reduction in cases has been appreciated, in Israel for example, in Hepatitis A infections.

Incidence in the case of Argentina, even after vaccination which reduced incidence by 88% was detected to be 10.2/100,000 and viral hepatitis infections still highly prevail in endemic populations such as Egypt, with the highest worldwide prevalence of HCV of 6 >40%, and poses future morbidity and mortality risks.

Incidence of hepatitis B virus infections can also be found, though minute, among blood donors even in developed countries such as Japan and the United States of America.

Drug-induced hepatitis remains a major concern to Medical practitioners.

In a survey, 13% of new patients who had anti-Tuberculosis administration had drug-induced hepatitis after treatment. Epidemiological studies made in Tayside in a ten year period

revealed 4992 patients with only viral hepatitis, of whom some were identified to have used drugs of potential abuse.

Current Management of Liver Diseases

Management of liver diseases involves the management of jaundice (since bilirubin is a Waste product which can be toxic to the system) and management of the root cause of the jaundice, then the cause of the liver disease. Hepatoprotectants used for the management of hepatitis varies from orthodox through homoeopathy to botanic medical therapies.

Silymarin, multivitamins, methionine, ursodeoxycholic acid and liver hydrolysate have also been used to manage liver diseases.

Nitric oxide, a cytoprotectant, inhibits cell destruction by modulating heat shock proteins, S-nitrosylatingcaspases at their catalytic site cysteine residue, triggering the cGMP pathway, and preventing mitochondrial dysfunction.

Presently, there hasn't been found any synthetic hepatic damage remedy safe enough to give therapy effectively, yet without severe side effects. In addition, no hepatic damage remedy has been found to give complete and perpetual cure to hepatic injuries, without relapses or resurfacing of the disease. Medicinal products used are found to give only symptomatic relief to patient with hepatic disorder without managing the fundamental cause to the symptoms.

In Homoeopathy, liver injury, depending on its symptoms, cause and extent of damage, ismanaged by a variety of drugs, some of which are Bryonia, Mercurius, Podophyllum, Chelidonium and Digitalis.

Natural hepatoprotectants are used, and though not well investigated, are claimed to be effective in controlling hepatic disorders while limiting the side effects of the drug.

Botanically, many hepatoprotectants have been reported. Glycosmisarborea extract washable to overcome the toxic effects of hepatotoxic agents in terms of lowering the levels of serum GPT, alkaline phosphatase necrosis of liver produced by carbon tetrachloride was reversed by the extract.

Intake of purple grape juice is found to possess antioxidant ability. Even its antioxidant ability is investigated to be more pronouncing in juices made from grapes cultivated with organic material than in purple grape juices of conventional sources. This may predict the possible effects of biochemically functional foods.

Dietary fish oil is also used to protect the liver from disorders, since it is known to contain omega-3. Studies with mice revealed that very long chain omega-3 PUFA like eicosapentaenoic and docosahexaenoic acid may act as preventive agent for hepatic cirrhosis.

New targets of hepatoprotectant still emerge, as the search of hepatoprotectants continues. In a recent report, the hepatic apelin system (Apelin is a peptide in serum that plays an important role in myophysiology and pathophysiology and inflammation), is evaluated (in rats with cirrhosis and ascites) for the involvement of the endogenous apelin system in the pathogenesis of the hepatic remodeling and complications that occur in advanced liver diseases. Findings predicted the hepatic apelin system as a novel therapeutic target in liver disease screened functionalized 1, 3-teraryls, synthesized through ring transformation of 6-aryl-3-carbomethoxy-4-methylthio-2H-pyran-2-one from arylketone for their hepatoprotective activity, and of them have demonstrated significant protection in animal hepatitis models.

In spite of the prevalence and increasing incidence and risk of hepatitis infections, there is however only a limited number of orthodox drugs and a limited number of botanical medicines with scientifically validated potential for the management of jaundice associated liver diseases. The use of herbal remedies for various ailments, folkloric or scientific has been of great usefulness to mankind. The search of botanical sources for hepatoprotective remedies to support the management of liver diseases will therefore be worthwhile. Spondias mombin extract is a frequently used medication However, its specific role in the management of jaundice has not been validated scientifically. There is also little knowledge on the potential in-vivo toxicity of the plant. This study intends to establish the scientific basis and to validate the use of the plant in the treatment of jaundice, and evaluate its potential toxicity to ensure the safety of the remedy.

Hepatoprotective Herbs

Herbal-based therapeutics for liver disorders has been in use in India for a long time and has been popularized world over by leading pharmaceuticals. Despite the significant popularity of several herbal medicines in general, and for liver diseases in particular, they are still unacceptable treatment modalities for liver diseases.

The limiting factors that contribute to this eventuality are:

1. lack of standardization of the herbal drugs;
2. lack of identification of active ingredient(s)/principles(s);
3. lack of randomized controlled clinical trials (RCTs), and
4. Lack of toxicological evaluation.

The use of natural remedies for the treatment of liver diseases has a long history, starting with the Ayurvedic treatment, and extending to the Chinese, European and other systems of traditional medicines. The 21st century has seen a paradigm shift towards therapeutic evaluation of herbal products in liver disease models by carefully synergizing the strengths of the traditional systems of medicine with that of the modern concept of evidence-based medicinal evaluation, standardization and randomized placebo controlled clinical trials to support clinical efficacy.

The present review is aimed at compiling data based on reported works on promising phytochemicals from medicinal plants that have been tested in hepatotoxicity models. The hepatoprotective activity is probably due to the presence of flavonoids in all few herbal plants. The results of this study indicate that extracts of leaves and plants extracts of some medicinal plant have good potentials for use in hepatic disease. The present review study give evidential explore mechanism of action of medicinal plants against experimentally induced hepatotoxicity. Hence the review study is concluded that the herbal drug possesses hepatoprotective activity and it has been proved by different animal models give many links to develop the future trials.

Medicinal Plants

Andrographolide and Neoandrographolide

Andrographolide and neoandrographolide are obtained from Andrographis paniculata Nees (Family: Acanthaceae), a well-known plant for liver diseases.

The plant is basically originated from south-east Asia and commonly called; Chuan Xin lian in China, Kalmegh and Bhunimba in India, Hempedubumi in Malaysia, etc.

the plant is also known as ‘‘king of bitters’’ due to its bitterness.
Bioguided phytochemical investigation of A. paniculata yielded andrographolide as the main hepatoprotective principle. Methanolic extract of A. paniculata showed 32% recovery in CCl4 induced liver damage in rats.
Andrographolide exhibited protective effects comparable to that of silymarin against liver damage in rats induced by carbon tetrachloride, paracetamol, galactosamine and t-butylhydroperoxide. Andrographolide, andrographoside, and neoandrographolide protect liver against the hepatotoxins by reducing the levels of the lipid oxidation product, malondialdehyde (MDA), and by maintaining high levels of the reduced form of glutathione (GSH).

Azadirachta Indica
Effect of *Azadirachta indica* leaf (Family of Meliaceae) extract on serum enzyme levels (glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acid phosphatase and alkaline phosphatase) elevated by paracetamol in rats was studied with a view to observe any possible hepatoprotective effect of this plant. It is stipulated that the extract treated group was protected from hepatic cell damage caused by paracetamol induction. The findings were further confirmed by histopathological study of liver. The antihepatotoxic action of picroliv seems likely due to an alteration in the biotransformation of the toxic substances resulting in decreased formation of reactive metabolites

Curcumin
Curcumin is a main component of rhizomes of ancient spice, turmeric (Curcuma spp. Family: Zingiberaceae).Turmeric is grown in warm and rainy regions of the world such as China, India, Indonesia, Jamaica, and Peru.
Apart from culinary use, turmeric has been used in traditional medicine for the treatment of jaundice and other disorders of liver, parasitic infections, ulcers, inflammation of joints, various skin diseases, etc. Curcuminoids are a mixture of several structurally close phenolic compounds present in the rhizomes of turmeric (approximately 3–5% w/w). Three Curcuminoids of major occurrence are Curcumin (60–80%), demethoxycurcumin (10–20%), and bisdemethoxycurcumin (5–10%).
The extracts of C. longa rhizomes exhibited protective activity against CCl4-induced liver injury *in vivo* and *in vitro*. Curcumin has a very good antioxidant activity. Most of its biological activities are considered due to this only.
It inhibits lipid peroxidation in rat liver microsomes, erythrocyte membranes and brain homogenates.
It is believed that the hepatoprotective activity of Curcumin is due to its antioxidant activity which is comparable to vitamins C and E.

Flacourtia Indica
The extracts of the aerial parts of *Flacourtia indica* (Burm. f.) Merr. Were evaluated for hepatoprotective properties. In paracetamol-induced hepatic necrosis in rat models, all extracts were found to reduce serum aspartate transaminase (AST), serum alanine transaminase (ALT) andserum alkaline phosphatase (ALP).
The most significant reduction of the serum level of AST and ALT were exhibited by petroleum ether and ethyl acetate extracts at a single oral of 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. On theother hand, the methanol extract did not show any remarkable effect on paracetamol-induced hepatic necrosis.
The hepatoprotective effects exhibited by petroleum ether and ethyl acetate extract might be mediated through the inhibition of microsomal drug metabolizing en-zymes.But, in this study the dose they have used is too high and it is not successful or rationale for human dose.

Glycyrrhizin
Glycyrrhizin, is a major and active constituent of roots of *Glycyrrhiza glabra* (Family: Leguminacae) commonly known as Indian licorice. It is a most commonly used herb in the traditional medicine system of India, China and other countries.
Glycyrrhizin prevents several forms of experimental liver injury in animals. It has shown hepatoprotective activity in animal models against carbon tetrachloride induced toxicity and hepatitis.
The hepatoprotective activity of glycyrrhizin has been attributed to its lipid peroxidation inhibitory, antioxidant, anti-inflammatory, and immunomodulatory activities. It enhances hepatic glucuronidation and activates P450 phase I detoxification reactions in animals.

Phyllanthin and Hypophyllanthin
Phyllanthin and hypophyllanthin are potent hepatoprotective lignans found in *Phyllanthus niruri Linn.* (Family: Euphorbiaceae).
The plant is commonly known as ‘‘Bhuiamliki’’ in India and ‘‘Look Tai Bai’’ in Thailand.
It is a wellknown Ayurvedic plant used in folk remedy for jaundice and other liver disorders. Chemically, both phyllanthin and hypophyllanthin are lignans.
Phyllanthin is linked through C8–C80 of phenyl propanoid units, while hypophyllanthin is additionally linked through C2–C70 to make a tetrahydronaphthalene ring system.
The plant has been effective against infective hepatitis and other disorders of liver.
The hexane fraction of the ethanolic extract showed potent hepatoprotective activity. Its liver protective effects have been established by various *in vitro* and *in vivo* experiments in rats and mice.
Both phyllanthin and hypophyllanthin protect liver against carbon tetrachloride and galactosamine-induced cytotoxicity in primary cultured rat hepatocytes. The liver protective effect of phyllanthus extract was due to free radical scavenging activity.

Picroside and Kutkoside
Picroside and kutkoside are active constituents of roots and rhizomes of Picrorrhiza kurroa Royle (Family: Scrophulariaceae), commonly known as ‘‘Kutki’’ or ‘‘Kutaki.’’ P. kurroa is a low, hairy herb with a perennial woody rhizome.

It is endemic to the Himalayan region and grows from Kashmir to Sikkim at an altitude of 3,000–5,000m. A bitter extract obtained from the rhizomes has been widely used in traditional medicine for the treatment of liver diseases.
''Picroliv,'' a combined formulation of picroside I and kutkoside has been developed as a potent hepatoprotective drug.
Picroliv is an enriched iridoid glycoside fraction containing at least 60% of 1:1.5 mixture (w/w) of picroside I, kutkoside and the remainder (40%) being a mixture of iridoid and cucurbitacin glycosides.
Picroliv showed curative in-vitro activity in primary cultured rat hepatocytes against toxicity induced by thioacetamide, galactosamine, and CCl4. Picroliv antagonizes paracetamol-induced lowering in LDL receptor cell surface expression and increases conjugated dienes in hepatocytes.

Rubia Cordifolia
Rubiadin isolated from *Rubia cordifolia* Linn, (Family of Rubiaceae) at a dose of 50, 100 and 200 mg/kg was administered orally once daily for 14 days in rats. The substantially elevated serum enzymatic activities of serum GOT, GPT, ALP and GGT; decreased activities of glutathione Stransferase and glutathione reductase were restored towards normalization in dose dependent manner which were induce by CCl4 treatment in rats. It also significantly prevents the elevation of hepatic MDA formation and depletion of reduced GSH content in the liver.

Silymarin
Silymarin, derived from the seeds of *Silybum marianum* L. (Family: Asteraceae or Compositae), is a member of sunflower family and commonly called milk thistle. The plant has been used for centuries as a natural remedy for liver and biliary tract diseases.
Milk thistle protects and regenerates the liver in most liver diseases such as cirrhosis, jaundice, and hepatitis.
It acts as preventive medicine which protects liver cells from incoming toxicants such as alcohols, drugs, medications, mercury and other heavy metals, pesticides, etc., and cleanses the liver from these harmful chemicals.
The active extract of S. marianum, known as silymarin, is amixture offlavanolignans namely; silibinin, silydianin, and silychristine. Although, the whole plant is used as medicinal, but seeds contain the highest content of Silymarin.
Silibinin is the most active constituent in silymarin mixture. It showed antihepatotoxic activity against Amanita phalloides, ethanol, paracetamol (acetaminophen) and carbon tetrachloride induced liver injury.

Solanum Nigrum
The effects of *Solanum nigrum* (Family of Solanaceae) extract (SNE) was evaluated on
Thioacetamide (TAA) induced liver fibrosis in mice. Mice in the three TAA groups were treated daily with distilled water and SNE (0.2 or 1.0 g/kg) via gastrogavage throughout the experimental period. SNE reduced the hepatic hydroxyproline and L- smooth muscle actin protein levels in TAA treated mice. SNE inhibited TAA induced collagen (L1) (I), transforming growth factor-M1 (TGF-M1) and mRNA levels in the liver. Histological examination also confirmed that SNE reduced the degree of fibrosis caused by TAA treatment. Oral administration of SNE significantly reduces TAA induced hepatic fibrosis in mice, probably through the reduction of TGF-B1 secretion

Taraxacum Officinale
Traditionally *Taraxacum officinale* has been used as a remedy for jaundice and other disorders ofthe liver and gall bladder, and as a remedy for counter acting water retention. Generally, theroots of the plant have the most activity regarding the liver and gall bladder.
Oral administration of extracts from the roots of *Taraxacum officinale* has been shown to act as a cholagogue, increasing the flow of bile. Bitter constituents like taraxecerin and taraxcin are active constituents of the medicinal herb.

Table: Review of Plant Used In the Treatment of Liver Disease.

Plant name	Plant part	Chemical constituents	Hepatoprotective action by
Adhatoda vasica	Leaves	asicine, vasicol, vasicinone, peganine, adhatodine, vasicolinone	Reduces elevated levels of SGOT and SGPT
Aloe barbadensis	Aerial parts	Barbaloin,chrysophanol,glycoside aloe‑emodin, glucose, galactose, mannose and galacturonic acid	Protects against increased lipid peroxidation and maintained glutathione contents by antioxidant property
Azadirachta indica	Leaves	Quercetin, rutin	Balances serum biochemical levels by antioxidant activity
Glycyrrhiza glabra	Roots	β‑Glycyrrhetinic Acid	Reduces the elevated levels of LDH, GOT, GPT and MDA and increases the reduced levels of SOD and GSH
Phyllanthus niruri	Leaves	Lignans, phyllanthin, flavonoids, Glycosides and tannins.	Inhibits membrane lipid peroxidation, Scavenges DPPH radical.
Terminalia chebula	Fruit	Chebuloside II	Antioxidant and act as membrane stabilizer
Vitis vinifera	Leaves	Halimane‑type diterpenes, vitetrifolins	Reduces MDA, AST, ALT and GSH Levels of plasma and liver tissue.

ALT‑Alanine transaminase, AST‑Aspartate aminotransferase, ALP‑Alkaline phosphatase, LDH‑Lactic acid dehydrogenase, GSH‑Glutathione Peroxidase, GR‑Glutathione reductase, GST‑Glutathione S‑Transferase, SOD‑Superoxide dismutases, TB‑Total bilirubin, MDH‑.Malate dehydrogenase, MDA‑Malondialdehyde, TG‑Triglyceraldehyde, CAT‑Catalase, LPO‑Lipid peroxidation,

DPPH‑2,2‑diphenylpicrylhydrazyl.SGOT‑Serum glutamic oxaloacetic transaminase, SGPT‑Serum glutamate pyruvate transaminase.

Recent Advances in Plant Hepatoprotectives: A Chemical & Biological Profile of Some Important Leads

Medicinal plants have been traditionally used for treating liver diseases since centuries. Several leads from plant sources have been found as potential hepatoprotective agents with diverse chemical structures.

Although, a big list of hepatoprotective phytomolecules was reported in the scientific literature, only a few were potent against various types of liver damages.

Of which, silymarin, andrographolide, neoandrographolide, curcumin, picroside, kutkoside, phyllanthin, hypophyllanthin, and glycyrrhizin have largely attracted the scientific community.

This review focuses discussion on the chemistry, biological activity,mode of action, toxicity, and future prospects of these leads.

The hepatoprotective potential of several herbal medicines has been clinically evaluated. Significant efficacy has been seen with silymarin, glycyrrhizin and Liv-52 in treatment of hepatitis, alcoholic liver disease and liver cirrhosis.

Some Recent Leads

A. Cliv-92

Cliv-92 is presently emerging as a potent hepatoprotective agent isolated from the seeds of Cleome viscosa Linne (Family: Capparidaceae).

Basically, it is a mixture of three structurally similar coumarinolignoids, Cleomiscosins A, B and C.

Cliv-92 was potent against carbon tetrachloride and phalloidin induced liver damage in rats. Its hepatoprotective activity was found to be comparable to Silymarin.

B. Oleanolic Acid

Oleanolic acid, a triterpenic acid found in weed Lantana camara Linn. (Family: Verbenaceae), a native to tropical regions.

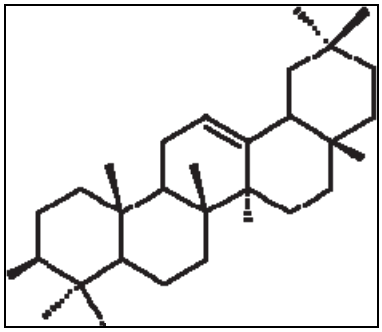
The plant is commonly known as ‘‘Kew bug,’’ ‘‘lantana,’ ‘‘cherry pie,’’ ‘‘Tick berry,’’ etc., in different regions.

Oleanolic acid has also been reported from several other plants like Syzygium aromaticum L., Ocimum basilicum L., Salvia triloba L., etc.

It has been found effective at inhibiting carbon tertrachloride induced liver injury.

Its effect is associated with the inhibition of carbon tertrachloride biotransformation by

The reduced expression of P450.

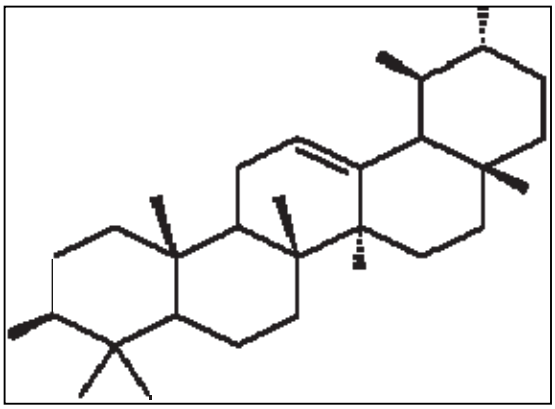


C. Ursolic Acid

Ursolic acid is a common triterpenic acid found in the leaves of Eucalytus tereticornis, Salvia triloba, Vinca minor, Ocimum basilicum, etc.

It has been reported to have hepatoprotective activity against carbon tetrachloride, ethanol, thiacetamide, and galactosamine damaged liver in rats.

Its hepatoprotective action was found to be comparable with silymarin.



D. Berberine

Berberine is an isoquinoline alkaloid obtained from the roots, rhizomes and stembark of

Berberis aristata (Family: Berberidaceae), commonly known as ‘‘barberry. The oxidative damage induced in the hepatocytes by tert-butyl hydroperoxide (t-BHP) was inhibited by berberine probably due to its antioxidant potential.In another study, the hepatoprotection activity is also believed to stem from its inhibitory effects on the ion channels of potassium and calcium in the rat hepatocytes.

Conclusion

It is showed that many herbs have potential to treat different induced of hepatic diseases especially *Silybum marianum* and *Phyllanthus niruri*. Phytochemicals obtained from herbs can provide as suitable main compounds for effective hepatoprotective agents such as antioxidant, anti-inflammatory and antiviral properties. Herbs either single or combination should possess adequate efficacy to treat severe induced hepatic diseases caused by alcohol, viral and drugs. The class of phytochemicals in herbs such as flavanoids and terpernoids received extensive attention due to their diverse pharmacological properties especially in hepatic diseases. Antioxidants play crucial role in inhibiting and scavenging radicals which eventually providing protection to human against hepatic diseases. In the future, the effective formulations for the combinations of phytochemicals have to be developed using original medical plants which proper pharmacological experiments and clinical trials. These combinations will promote to treat various inducing factors of hepatic diseases.

- Chronic hepatic diseases stand as one of the foremost health troubles worldwide, with liver cirrhosis and drug induced liver injury accounting ninth leading cause of death in western and developing countries.
- Therapies developed along the principles of western medicine are often limited in efficacy, carry the risk of

adverse effects, and are often too costly, especially for the developing world. Therefore, treating liver diseases with plant-derived compounds which are accessible and do not require laborious pharmaceutical synthesis seems highly attractive.

- In this project, an attempt has been made to compile the reported hepatoprotective plants from India and abroad and may be useful to the health professionals, scientists and scholars working the field of pharmacology and therapeutics to develop evidence-based alternative medicine to cure different kinds of liver diseases in man and animals.

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