International Journal for Pharmaceutical Research Scholars (IJPRS)

V-6, I-2, 2017 ISSN No: 2277 - 7873

REVIEW ARTICLE

A Mini Review: Hepatoprotective Natural Products

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Manuscript No: IJPRS/V6/I2/00050, Received On: 18/05/2017, Accepted On: 24/05/2017

ABSTRACT

Liver is a vital organ play an important role in metabolism and disposition of chemicals (xenobiotics) from the body. Liver disease may cause liver inflammation or tissue injury and affects liver physiologic condition. The available synthetic drugs to treat liver disorders may cause many side effects and also cause further damage to the liver. Therefore, Herbal drugs have become increasingly popular and their use is spread in world - wide. The natural plants contain several photochemical which possess antioxidant z property; leading to anti - hepatotoxic activity. It is aimed on promising Phytochemical from natural plants that have been tested in hepatotoxicity models using modern scientific system.

KEYWORDS

Carbon tetrachloride (CCL4), Hepatotoxicity, serum alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and alkaline phosphatase (ALP).

INTRODUCTION

In recent years, researchers have seen the activity of plants and indigenous healers used traditionally to support liver function and treat diseases of the liver. In India, a number of natural plants and their preparation are used to treat hepatic disorders.[1] Liver is the key organ in the metabolism, detoxification, and secretary functions in the body, and it have numerous disorder with no effective cure, so researcher find new medicine for hepatic disease. Many formulations from plant origins have been used for treatment of liver diseases.[2] Livser diseases are among the most serious ailment. They may be classified as acute or chronic hepatitis (inflammatory liver diseases), hepatosis (non inflammatory diseases) and cirrhosis (degenerative disorder resulting in fibrosis of the liver). Disarrangement to the liver imposed by hepatotoxic agents is of serious issue. There is an ever increasing need of a formulation which could protect it from such disarrangement.[3] The natural plants have many phytoconstituent, which possess antihepatotoxic activity. Hence, hepatoprotective natural products such as Silybum marianum, Andrographis paniculata, Trianthema portulacastrum Linn., Premna tomentosa Linn., Tamarindus indica Linn., Glycyrrhiza glabra, Phyllanthus emblica Linn., Lygodium flexuosum Linn., Curcuma longa, Solanum nigrum, Tephroia purpurea, Azadirachta indica, Scutellaria rivularis, Colchicum autumnale, Cassia roxburghii, Hedyotis corymbosa Linn., Coccinia grandis, Cistanches salsa, Anoectochilus formosanus and Terminalia catappa, etc. is reviewed.

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1. Silybum marianum

Silybum marianum, is also known as 'milk thistle' (belonging to family Asteraceae/Compositae), is one of the oldest researched plants in the treatment of liver diseases. Silymarin (a) is extracted from the dried seeds of milk thistle plant; dried seeds have higher concentration of silymarin than other part of the plant. Silymarin is a complex mixture of four flavonolignan isomers, namely silybin, isosilybin, silydianin and silychristine with an empirical formula $C_{25}H_{22}O_{10}$. Silymarin have structural similarity with steroid hormones and it is responsible for its protein synthesis. Amongst the flavonoids, which have proven antioxidative, antiviral or anticarcinogenic properties like glycyrrhizin, phyllanthin, silybin, picroside and baicalein, can introduce as primary compounds for further development as hepatoprotective drugs.[4, 5]

2. Andrographis paniculata

Andrographis paniculata (Family of Acanthaceae) have a chemical constituent andrographolide B methanolic extract (equivalent to 100 mg/kg of andrographolide) and 761.33 mg/kg IP, of the andrographolide free methanolic extract of the plant, using CCl_4 - induced toxicity in rats. Biochemical parameters like, serum transaminases - GOT and GPT, serum alkaline phosphatase, serum bilirubin and hepatic triglycerides were evaluated to estimate the liver function. The result shows that andrographolide is the major active antihepatotoxic principle present in Andrographis paniculata[6].

3. Trianthema portulacastrum Linn.

Trianthema portulacastrum Linn (Family of Aizoaceae) is a prostrate, glabrous, succulent annual plant. It is found as a weed in cultivated and waste lands almost throughout India. The ethanolic extract of Trianthema portulacastrum L. gives a significant dose dependent protective effect against paracetamol and thioacetamide induced hepatotoxicity in albino rats. In case alcoholic poison also acts as an antidote[7] and showed favorable effect in the reduction of DENA-induced hepato carcinogenesis[8].

4. Premna tomentosa Linn.

Premna tomentosa Linn. (Family of Verbanaceae), also called as 'Pudangainari' and 'Krishnapalai' is a herbal medicinal plant used for the treatment of various diseases. The methanolic extract of Premna tomentosa leaves have antioxidant[9] property gives significant activity against acetaminophen - induced hepatotoxicity in rats[10]. The hepatoprotective activity of the plant due to the presence of antioxidant compound limonene in the plant.

5. Tamarindus indica Linn.

Tamarindus indica Linn. is commonly known as tamarind (belonging to the family of Fabaceae). It is a tropical tree, found in Africa and Southern Asia. The mostly constituents of the tamarind are antioxidants so for this reason it has been used for centuries as hepatoprotective. By the inhibition of ROS (Reactive oxygen species) mechanism formation, it shows strong antioxidant activity of the polyphenols and flavonoids.[11, 12] The Essential oils of the tamarind given antioxidant effects are strongly dependent on the content of phenolic acid.[13] Ferulic acid protects from CCl_4 induced acute liver injury through reduction of oxidative damage.[14]

6. Glycyrrhiza glabra

Glycyrrhizin C is an aqueous extract of the liquorice root (Glycyrrhiza glabra) and used to treat bronchitis, jaundice and gastritis from ancient time in traditional medicine. The main phytoconstituent are flavanoids, glycyrrhetic acid, hydroxycoumarins, and betasitosterol. In Japan, a standard extract of the glycyrrhizin containing, cysteine and glycine used to treat chronic hepatitis as stronger neominophagen C (SNMC). Treatment with Glycyrrhizin with 80 mg/kg/day administration I.V for 2 week lowered the higher level of alanine transaminase.[15] In the United State SNMC mainly available as tablet, liquid and powder. In cell culture experiments, glycyrrhizin blocks sialylation of hepatitis B surface antigen and modifies glycosylation

leading to its retention in the trans-golgi apparatus.[16]

7. Phyllanthus emblica L.

Phyllanthus emblica Linn. is traditional medicine using for the treatment hepatic disease.[17] Researcher have given the hepatoprotective property of Phyllanthus emblica (PE) against CCL_4[18] and paracetamol.[19] PE contains rich amount of tannin and flavonoids which shows the antioxidant activity.[20] The present study aims to investigate the protective effect of 50% ethanol extract of PE on rat liver damage induced by ethanol and also the possible mechanisms of PE hepatoprotection.

8. Lygodium flexuosum Linn.

Lygodium flexuosum Linn. (belonging to the family Lygodiaceae), is a climbing fern found throughout the Western Ghats of Kerala, India. The roots, rhizomes and leaves part of the plant are useful in the treatment of jaundice.[21, 23] Several chemical compounds such as dryocrassol, tectoquinone, sitosterol, kaempferol, kaempferol -3-d-glucoside, stigmasterol and O - P - coumaryl - dryocrassol are present in the plant.[23] Peroxidative damage to liver microsomes and hepatocytes prevented through these compounds.[24, 29] In the present study Lygodium flexuosum n - hexane extract was used in acute liver injury model against carbontetrachloride (CCl_4) in preventive and curative treatments as antihepatotoxic activity.

9. Curcuma longa

Turmeric has been protective property for animal livers from a variety of hepatotoxic substances, including carbon tetrachloride, pentobarbitol, 1-chloro-2, 4- dinitrobenzene, and paracetamol. Diaryl hepatonoids including Curcumin is the active constituent of the plants. Curcumin D, is the main constituent of Curcuma longa which is the yellow pigment of turmeric have antioxidant property. At the dose of 600 mg/kg, paracetamol induced liver damage in rats as barefaced by significant increase in serum alanine amino transferase (ALT), Aspartate amino transferase (AST) and alkaline phosphatase (ALP).[30]

10. Solanum nigrum

Solanum nigrum (Family of Solanaceae) is known as kakamachi. Aromatic water extracted from the drug is widely prescribed by herbal vendors for liver disorders.[31] Solanum nigrum extract (SNE) was verified on thioacetamide (TAA) induced liver fibrosis in mice. Mice categorized in the three TAA groups and then daily treated with distilled water and SNE (0.2 or 1.0 gm/kg) through gastriclavage throughout the experimental period. SNE decrease the level of hepatic hydroxyproline and α - smooth muscle actin protein levels in TAA treated mice. SNE prevented TAA induced collagen, transforming growth factor - M1 and mRNA levels in the liver. Oral administration of SNE decreases TAA induced hepatic fibrosis in mice, by the reduction of transforming growth factor - M1 secretion.[32]

11. Tephroia purpurea

In Ayurveda, the plant is known as sharpunkha. Alkali preparation of the drug is commonly used in treatment of liver and spleen diseases. In animal models, it offered protective action against carbon tetrachloride and D – galactosamine poisoning.[33]The roots, leaves and seeds contain tephrosin, deguelin and quercetin (e). The hepatoprotective constituent of the drug is still to be proved.

12. Azadirachta indica

Azadirachta indica leaf (belonging to family Meliaceae) extract effect was obseved on serum enzyme levels (glutamate oxaloacetate transaminase, acid phosphatase, glutamate pyruvate transaminase and alkaline phosphatase) increased through paracetamol in rats was studied and then observe any possible hepatoprotective activity of this plant. It is specified that the extract treated group was protected from hepatic cell damage (by paracetamol induction). The researchers were at a

greater extent proved by histopathological study of liver. The anti - hepatotoxic action of picroliv seems contingent due to changes in the biotransformation of the toxic substances resulting in reduced formation of reactive metabolites.[34]

13. Scutellaria rivularis

Scutellaria rivularis Benth (Family of Labiatae) have three major components (Baicalein F, Baicalin and Wogonin) isolated from entire plant. Wogonin (5 mg/kg I.P) shows more effect in CCl_4 and D - GalN treated rats. Baicalein and Baicalin at the dose 20 mg/kg IP in D - GalN (galactosamine) and APAP (acetyl - para - aninophenol), at dose 10 mg/kg IP in CCl_4 treated rats exhibit best effect. Protective effects were seen through comparing the serum GOT, GPT and histopathologic examination.[35]

14. Colchicum autumnale

Colchicum autumnale (Family of Colchicaceae) have the major alkaloid Colchicine G, it protects the liver of experimental animals against many hepatotoxins namely D - galactosamine and paracetamol through its affability to bind microtubule protein. Trimethylcolchicinic acid (TMCA) a colchicine derivative that does not bind tubulin protein to WIT (waterflow identification test) tested on chronic liver damage induced through CCl_4 and through bile duct ligation (BDL). So, both compounds were evenly powerful but that TMCA could be administered at larger doses than colchicines without side effects and better hepatoprotective actions.[36]

15. Cassia roxburghii

Seeds of Cassia roxburghii (Family of Fabaceae) have hepatoprotective activity so had been used in ethnomedicine for several liver disorders. The methanolic extract of Cassia roxburghii invert the toxicity outcome via ethanol CCl_4 combination in dose dependent manner in rats. The extract at the doses of 250 mg/kg and 500 mg/kg are comparable to the effect produced by Liv-52®, a proper accepted plants based hepatoprotective formulation against hepatotoxins.[37]

16. Hedyotis corymbosa Linn.

Hedyotis corymbosa Linn. (Family of Rubiaceae) is a weed, mostly found throughout India. Hedyotis corymbosa have hepatoprotective effects have been investigated on carbon tetrachloride (CCl_4) induced liver damage in rats.[38, 39] A literatures discloses its hepatoprotective effects on paracetamol induced liver damage. It shows activity in jaundice and several diseases of the liver, vitiated conditions of pitta, giddiness, dyspepsia, colic, constipation, heat eruptions, helminthiasis, skin diseases, cough, bronchitis, hyperdypsia, necrosis, nervous depression caused by hepatopathy.[40]

17. Coccinia grandis

Coccinia grandis Linn. (Family of Cucurbitaceae) fruits alcoholic extract was evaluated in CCl_4 induced hepatotoxicity in rats and evaluated the levels of AST, ALT, ALP, total proteins, total and direct bilirubin. The activities of serum enzymes (AST, ALT and ALP) and bilirubin significantly ($p<0.05$) decreased. At a dose level of 250 mg/kg, the alcoholic extract, which were comparable to that of silymarin[41] disclose its hepatoprotective effect.

18. Cistanches salsa

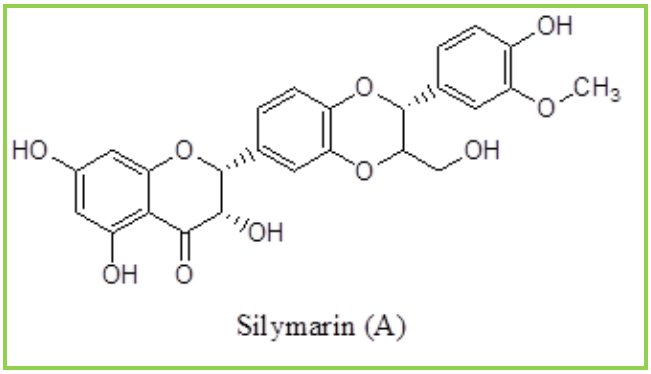
Cistanches salsa (belonging of Orobanchaceae), have a constituent Echinacoside H, (50 mg/kg, I.P) is a phenylethanoid isolated from the stems show disinfectant result by decreasing serum ALT, AST levels, hepatic methyl di-oxyamphitamine (MDA) content, ROS production, and hepatic superoxide dismutase(SOD) activity and GSH content in carbon tetrachloride - induced hepatotoxicity were restored remarkably in rats. Echinacoside treatment were also significantly improved the histopathological damage of liver and the number of apoptotic hepatocytes.[42]

19. Anoectochilus formosanus

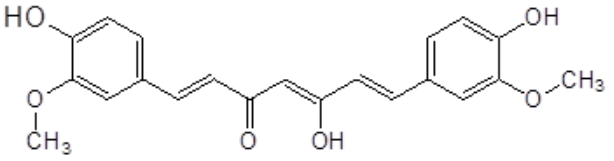
Anoectochilus formosanus (Family of Orchidaceae) fresh whole plant aqueous extracts (AFEW - 2) at dose 130 mg/kg inhibited chronic hepatitis (induced by CCl_4) in mice by decreasing the level of SGPT and hepatic hydroxyproline and also prevented the hypoalbuminemia and splenomegaly. In an in vitro study, the LD50 values for H_2O_2-induced cytotoxicity in normal liver cells were significantly higher after kinsenoside pretreatment at the dose 20 - 40 µg/ml.[43]

20. Terminalia catappa

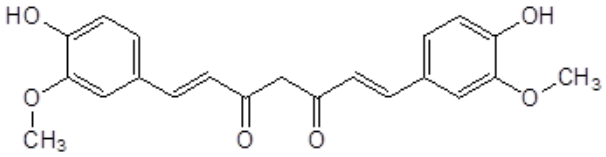
Terminalia catappa Linn, (Family of Combretaceae) have a constituent Punicalagin I and Punicalin isolated from the leaves inhibited hepatitis by decreasing levels of AST and ALT which increased by APAP administration in rats.[44]



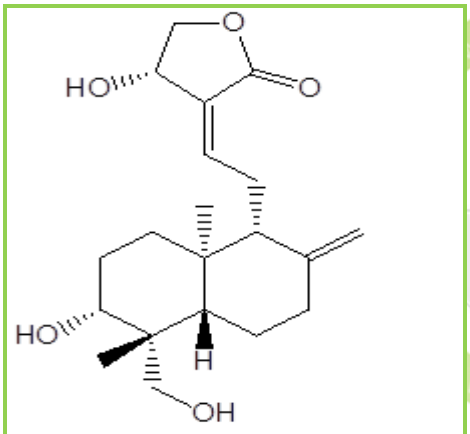
Silymarin (A)



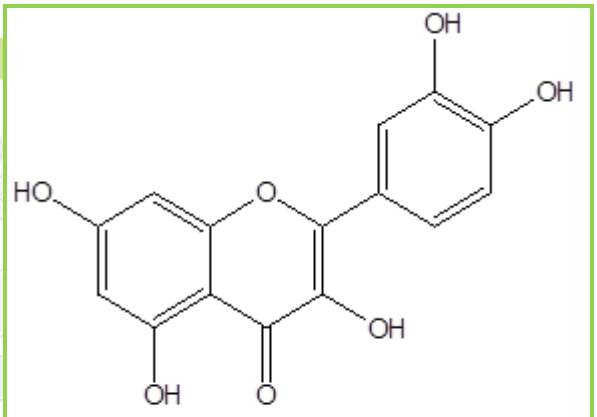
Curcumin D- Enol form



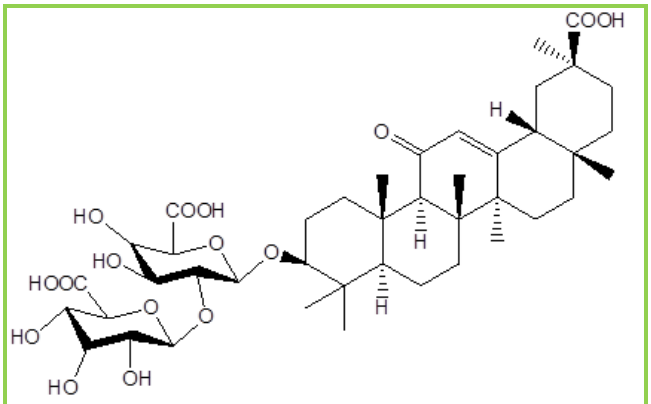
Curcumin D-Keto form



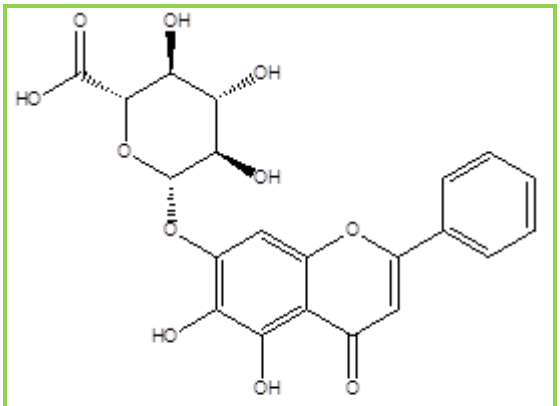
Andrographolide (B)



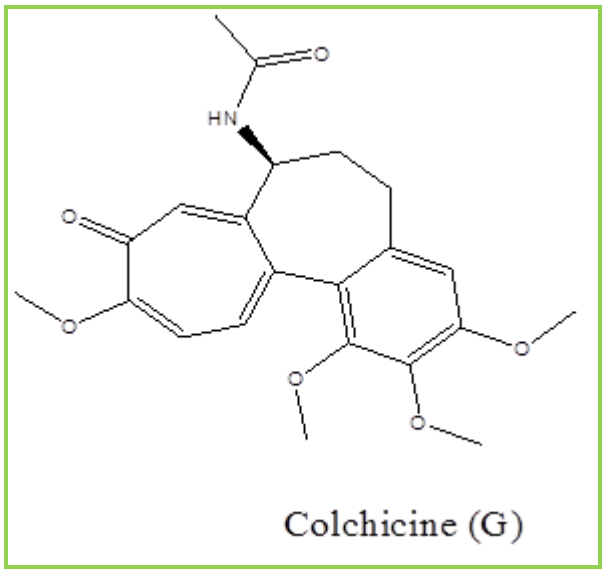
Quercetin (E)



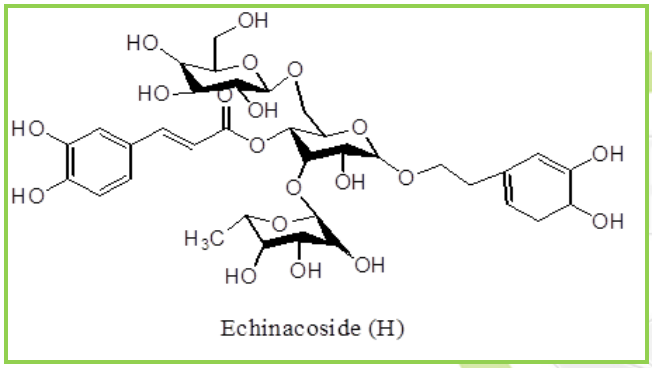
Glycyrrhizic acid (C)



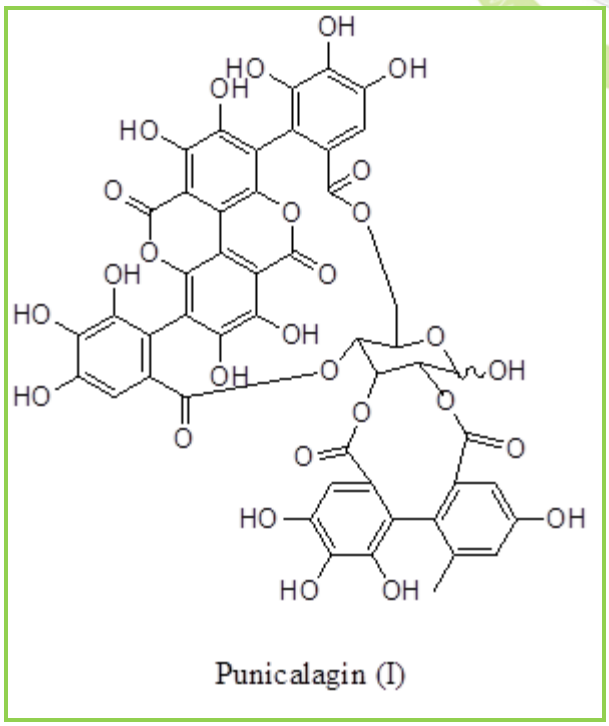
Baicalin (F)



Colchicine (G)



Echinacoside (H)



Punicalagin (I)

CONCLUSION

This review article attempt to collect and assemble the details about few hepatoprotective medicinal plants, which will be useful to our society, to travel in to a field of other systems of medicine. A more thorough review on various herbal products available in India and abroad as a hepatoprotectant is in near future. This article in order to shows the usefulness of the various medicinal plant as hepatoprotectant.

ACKNOWLEDGMENT

This review is written in dedication of the God almighty for blessing me with the peace of mind, courage and strength, also with affectionate dedication to my loving family members and my dear friends who throughout the year have given me lot of encouragement, valuable ideas and timely support whenever needed.

I am very thankful to Director, HOD and all faculty members of Goel Institute of Pharmacy & Sciences, Lucknow, for their technical support and most valuable guidance throughout my review article.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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HOW TO CITE THIS ARTICLE

Singh, J., Sachin, V. (2017). A Mini Review: Hepatoprotective Natural Products. *International Journal for Pharmaceutical Research Scholars (IJPRS)*, 6(2), 81-89.

