Review Article



Review on Herbal Plants with Hepatoprotective Activity Against Alcohol Inducing Liver Cirrhosis

K. Madhavi,¹ G. Yaswanth Reddy ^{*1}, P Chinna Srinivas¹, K. Navya Sri², E. Likitha³, S. Arfiya⁴, J Naga Lakshmi⁵

1. Assistant Professor, Department of Pharmacology, Vignan Pharmacy College, Jawaharlal Nehru Technological University, Vadlamudi 522213, Andhra Pradesh. India.

2 UG Student Department of Pharmacology, Vignan Pharmacy College, Jawaharlal Nehru Technological University, Vadlamudi 522213, Andhra Pradesh, India.

3. UG Student Department of Pharmacology, Vignan Pharmacy College, Jawaharlal Nehru Technological University, Vadlamudi 522213, Andhra Pradesh, India.

4. Department of Pharmacology, Vignan Pharmacy College, Jawaharlal Nehru Technological University, Vadlamudi 522213, Andhra Pradesh, India. 5 Associate professor and HOD, Department of Pharmacology, Vignan Pharmacy College, Jawaharlal Nehru Technological University, Vadlamudi 522213, Andhra Pradesh, India.

*Corresponding author's E-mail: drjnlpharmacology@gmail.com

Received: 06-02-2024; Revised: 28-03-2024; Accepted: 10-04-2024; Published on: 15-04-2024.

ABSTRACT

Different combinations of plants and herbal extracts are most likely to provide desired activities or actions to cure different liver diseases. An approach to modern drug development can provide different valuable drugs but search for pure phytochemicals and drug form is more time consuming and expensive. Various polyherbal formulations and medicinal plants are used to treat and prevent various types of liver diseases. Herbal drugs are broadly used over than allopathic drugs for various hepatic disorders, due to less expensive, more acceptability, good compatibility with human body. Hepatic cirrhosis is a major health concern, it became a big challenging health care professionals and scientists. It is a life-threatening condition such as hepatitis, liver cirrhosis. Hepatic cells may get damaged. Hence hepatoprotective activity of herbal plants such as "eclipta alba", "Acacia confusa", "Curcuma longa", "Glycyrrhiza glabra", "solanum nigrum". Present review is aimed at collecting data on various medicinal plants that have proved for hepatoprotective activity in laboratory animal models.

Keywords: Hepatoprotective activity, Hepatotoxicity, Herbal drugs, Polyherbal formulations.

INTRODUCTION

iver disease is a major cause of illness and death which accounts for approximately 2 million deaths per year worldwide, in that 1 million deaths are due to complications of cirrhosis and 1 million is due to viral hepatitis and hepatocellular carcinoma. Liver diseases are steadily increasing over the years and World Health Organization (WHO) has projected it as the 12th most important cause of death in the world by 2030 and may be the 10th most common cause of death in India by 2040. In India about 10 lakh people are diagnosed with liver diseases every year and it affects every one in five Indians.

It is estimated that about 7,500 plants are used in local health traditions in rural and tribal villages of India. The classical systems of medicine such as Ayurveda, Siddha, Amchi, Unani and Tibetan use about 1,200 plants. ¹ Hence it is seeking the researchers' attention to find out the effective treatment strategies. Phytochemicals from natural resources are the main leads for the development of noble hepatoprotective drugs. The majority of the natural sources whose active compounds are currently employed actually have an ethnomedical use. Liver is the most vital organ, considered to be Centre of metabolism for nutrients such as carbohydrates, proteins, lipids and drugs. It also involved in excretion of waste metabolites and other xenobiotics. There by providing protection against foreign substances by detoxifying and eliminating through bile and urine. Injury to hepatocytes caused due to exposure of various toxicants such as chemotherapeutic agents, halothane and paracetamol. Enhanced lipid peroxidation in alcoholic people may result in development of hepatitis which may induce liver cirrhosis.

From decades onwards it was proved that plants are used for various cases of hepatic disorders similarly number of researchers are stated that hepatoprotective activity of many herbals like Terminalia arjuna, Pleurotus pulmonarias, Nigella sativa. He From decades onwards it was proved that plants are used for various cases of hepatic disorders similarly number of researchers are stated that hepatoprotective activity of many herbals like Terminalia arjuna, Pleurotus pulmonarias, Nigella sativa. Hence there is an ever-increasing need for safe hepatoprotective agent since there is an ever-increasing need for safe hepatoprotective agent².



Figure 1: Risk factors for liver diasease



Available online at www.globalresearchonline.net

Medicinal plants play a key role in the human health care. The traditional medicine refers to a broad range of ancient natural healthcare practices including folk/tribal practices as well as Ayurveda, Siddha, Amchi and Unani³. The selection of the plant species is a crucial factor for the ultimate success of investigation. Through random selection gives some hint, targeted collection based on chemotaxonomic relationships and ethnomedical information derived from tradition medicine are more likely to yield pharmacologically active compounds ⁴. Hepatic cirrhosis is a major health concern challenging health care professional and scientists This can be a lifethreatening condition that can lead to jaundice, hepatitis, abdominal pain, nausea, vomiting and, over time, cirrhosis of the liver. Detailed study and documentation of plants used in local health traditions and pharmacological evaluation of these plants and their taxonomic relatives can lead to the development of invaluable herbal medicines against many dreaded diseases. Random screening of plants has not been shown to be economically efficient Most of the hepatotoxic chemicals damage liver cells mainly by inducing lipid peroxidation and other oxidative damages in liver. It has been estimated that about 90% of the acute hepatitis is due to viruses ⁵. The major viral agents involved are Hepatitis B, A, C, D (delta agents), E and G. Of these, hepatitis B infection often causes chronic liver disease. Primary liver cancer has also been shown to be produced by these viruses ⁶.

Liver diseases and its metabolism:

Liver is the most prominent digestive gland that metabolizes drugs by oxidation, reduction, hydrolysis, condensation, conjugation, or isomerization. Two stages of hepatic drug metabolism convert drugs into conjugated water-soluble substances through Phase-I, and Phase -II metabolism, which are excreted either urine or bile. Due to lack of metabolism in liver, in disease condition, the drugs may induce the hepatotoxicity, apoptosis of hepatocytes, injury to bile duct, inhibition of mitochondria, and cytolytic T-cell activation. Various researches were done on herbals for their hepatoprotective activity, found highly efficacy against the drug induced hepatic toxicity. The manifestations of hepatotoxicity include weight loss, malaise, jaundice, dyspepsia, blood coagulation, oedema, and pruritus ⁷.



Figure 2: Important medicinal plants and their active ingredients

Table 1: Hepatoprotective activity of medicinal plants with part were used

| Name of the plant | Family | Part used | Active constituents | Mechanism of action |
|-------------------------------|----------------|-------------|---|--|
| Tinospora cardifolia | Menispermaceae | Whole plant | Saponarin Galactoarabinan | Increased GSH, CAT levels and reduce LPO enzyme ⁸ |
| Curcuma longa | Zingiberaceae | Rhizomes | Curcumin | Reduces liver enzymes like ALP, ALT 9,10 |
| Glycyrrhiza glabra | Fabaceae | Root | Glycyrrhizin, Isoliquiritin | Concentration dependent inhibition in cell growth of the HePG2 ¹¹ |
| Kleinhovia hospita | Sterculiaceae | Leaves | Eleutherol | It scavenged the radical ¹² |
| Morinda pubescens | Rubiaceous | Leaves | Hyoscyamine | DPPH Radical scavenging 13 |
| Asparagus racemosus | Liliaceae | Whole plant | Crude extract and purified aqueous fraction | Lipid peroxidation, Oxidation ¹⁴ |
| Rosmarinus officinalis L | Lamiaceae | Whole plant | Rosmanol, Carnosol | Increased anti-oxidant activity ¹⁵ |
| Semecarpus anacardium | Anacardiaceae | Nut | Anacardioside, Galluflavanone | Increase glutathione levels ¹⁶ |
| Symplocos racemosa | Symplocaceae | Bark | Symploquinone A, B, C | Increases glutathione, catalase and reduces LPO ¹⁷ |
| Cochlospermum angolensis | Bixaceae | Whole plant | Gallic acid, propocatechuic acid | Increased DPPH scavanging activity 18 |
| Berberis vulgaris | Berberidaceae | Whole plant | Cannabisin G | Lowers nitrous oxide levels 19 |
| Viscum album | Viscaceae | Whole plant | Viscumin | Stimulates lymphocytes 20 |
| Urtica dioica L | Urticaceae | Seeds | P- coumaric acid | Increase the level of anti-oxidants ²¹ |
| Acacia mellifera | Leguminosae | Leaves | Sterols, saponins, flavonoids | Cures tissue lesions of liver ²² |
| Catharanthus roseus | Apocynaceae | Whole plant | Vincristine | Induces anti-body protection ²³ |
| Adansonia digitata | Malvaceae | Leaf | Terpenoids, amino acids, vitamins, lipids | Minimize the necrosis and regeneration of hepatocytes ²⁴ |
| Lepidium sativum | Brassicaceae | seeds | Coumarins, saponins, Tri terpenes | Mild to moderate changes in hepatocytes ²⁵ |
| Nigella sativa | Ranunculaceae | seeds | Quinine, thymoquinone | Induces apoptosis and inhibit proliferation in PDA cells ²⁶ |
| Aegle marmelos correa | Rutaceae | Leaves | Marmin, umbelliferon | Suppresses lipid peroxidation (LPO), xanthine oxidase ²⁷ |
| Ficus pseudopalma blanco | Moraceae | Whole plant | Lupeol | DPPH, Nitric oxide and FRAP scavenging activity ²⁸ |
| C-Lansium(lour) | Rutaceae | Whole plant | 8-hydroxy psoralen | Increase DPPH and superoxide anion scavenging activity ²⁹ |
| Caesalpinia bonducella | Leguminosae | Whole plant | 5-hydroxy vihaticanal | Reduces lipid peroxidation ³⁰ |
| Terminalia arjuna | Combretaceae | Bark | Terminoside-A | Increase SOD, CAT, GSH, levels and reduce LPO enzyme $^{\rm 31}$ |
| Zingiber officinale roscoe | Zingiberaceae | Rhizome | Flavonoids, poly phenols | Decrease liver enzymes like bilirubin in plasma ³² |
| Fagonia schweinfurthii | Zygophyllaceae | Whole plant | Phenols and flavonoids | By inhibiting lipid peroxidation and increase in the anti-oxidant enzymatic activity ³³ |
| Origanum vulgare | Lamiaceae | Leaves | Terpenoids, tannins, saponins, phenolic compounds, flavonoids | By lowering the serum ALT, ALP and AST levels ³⁴ |
| Nerium oleander | Apocynaceae | Flower | Glycosides, terpenoids, flavonoids, saponins | By elevating level of SOD and decreasing level of MDA ³⁵ |



Available online at www.globalresearchonline.net

CONCLUSION

The hepatoprotective effect of the plants is mainly due to presence of secondary metabolites such as flavonoids, alkaloids, terpenoids, glycosides and steroids. Plant extracts for liver diseases have to possess sufficient efficacy to remedy extreme liver cirrhosis resulting from poisonous chemicals, viruses, alcohol consumption, as well as repeated uses of medication like paracetamol, rifampicin and isoniazid. There is no accurate treatment for liver cirrhosis in allopathic medicine system, only palliative therapy and surgical procedure. However, due to lack of donors it becomes less chance in economical poor people. Hence herbal agents like flavonoids, phenols, are significant hepatoprotective effective in treatment of liver cirrhosis caused by harmful chemicals.

Despite, most plant extracts are used by people in rural areas in developing countries for various complications. Hence herbal medications should be recommended within the setting of more finely-conducted clinical trials better education of both patients and doctors about herbal products seems to be needed. Finally, to produce more effective plant based hepatoprotective drugs it will be necessary to carry out further studies on the structural modifications of the active principles derived from herbal extracts using computational chemistry techniques. Our current review is focused on herbal plants with high hepatoprotective activity including active ingredients, it could be useful for researcher who are working on the hepatoprotective activity of novel compounds.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. J. Naga Lakshmi K. Mohana Rao, B. Siva, U. Mahendra, K. Vinay, A. Narendra Babu, Evaluation of Additive/Synergistic Effect of Piper nigram and Ocimum sanctum Extracts for their Antidepressant Activity, International Journal of Pharmaceutical Sciences Review and Research, 2021, 70;2;171-174.

2. Afaf I, Abuelgasim, Nuha HS, Mohammed AH. Hepatoprotective effect of Eclipta alba against carbon tetrachloride-induced damage in rats. Res J Animal Veterinary Sci. 2008; 3:20-23.

3. Aszalos A, Editor. Antitumor Compounds of Natural Origin. Boca Raton, CRC Press, 1982.

4. Absar Ahmed Qureshi, Prakash T et al. Hepatoprotective and Antioxidant activities of flowers of Calotropis procera (Ait) r. Br. in CCl4 induced hepatic damage. Indian J Exp Biology. 2007; 45:304-310.

5. J Naga Lakshmi, P Hemasoundarya, madhuri, Narendra Babu A, A Short review on liver cirrhosis, international journal of pharmaceutical and clinical research.2017,9(9); 638-641.

6. Smuckler EA. Alcoholic Drink: Its Production and Effects. Fed Proe 1975; 34:2038-44.

7. Schiano TD. Hepatotoxicity and complementary and alternative medicines. Clinical Liver Diseases 2003; 7:453-473.

8. Jayaprakash R, Ramesh V, Sridhar MP, Sasikala C. Antioxidant activity of ethanolic extract of *Tinospora cordifolia* on N-nitrosodiethylamine (diethyl nitrosamine) induced liver cancer in male Wister albino rats. J. Pharm. Bio allied Sci 2015;7(1): S40.

9. Ibrahim J, Kabiru AY, Adeleke TA, Lawal B, Adewuyi AH. Antioxidant and hepatoprotective potentials of curcuminoid isolates from turmeric (*Curcuma longa*) rhizome on CCl4-induced hepatic damage in Wistar rats. J Taibah Univ. Sci. 2020;14(1):908-915.

10. Shankar R, Rawat MS, Deb S, Sharma BK. Jaundice and its traditional cure in Arunachal Pradesh. J Pharma. Sci. Innova. 2012; 1:93-97.

11. Antioxidant activity and antiproliferative action of methanolic extract of liquorice (*Glycyrrhiza glabra*) in HepG2 cell line. Int. J Pharm. Pharm. Sci. 2016;8(9):293-298.

12. Arung ET, Kusuma IW, Purwatiningsih S, Roh SS, YangCH et al. Antioxidant activity and cytotoxicity of the traditional Indonesian medicine Tahongai (*Kleinhovia hospita* L.) extract. J Acupunct Meridian Stud2009.

13. Kumar DJ, Santhi RJ. Antioxidant and cytotoxic effects of hexane extract of *Morinda pubescens* leaves in human liver cancer cell line. Asian Pac. J Trop. Med2012;5(5):362-366.;2(4):306-308.

14. Jayashree P. Kamat A, Krutin K. Boloor A, Thomas P.A. Devasagayam A, S.R. Venkatachalam Bantioxidant Properties of *Asparagus racemosus* against Damage Induced By G-Radiation in Rat Liver Mitochondria, Journal of Ethnopharmacology 71 (2000) 425–435.

15. Vicente G, Molina S, González-Vallinas M, García-RiscoMR, Fornari T et al. Supercritical rosemary extracts, their antioxidant activity and effect on hepatic tumor progression. J Superscript Fluids 2013; 79:101-108.

16. Premalatha B, Sachdanandam P. *Semecarpus anacardium*. nut extract administration induces the in vivo antioxidant defense system in aflatoxin B1 mediated hepatocellular carcinoma. J Ethnopharmacol 1999;66(2):31-139.

17. Vijayabaskaran M, Yuvaraja KR, Babu G, Sivakumar P, Perumal P et al. Hepatoprotective and antioxidant activity of *Symplocos racemosa* bark extract on DMBA induced hepatocellular carcinoma in rats. IJCT 2010;1(3):147-158.

18. Pereira C, Calhelha RC, Barros L, Ferreira IC. Antioxidant properties, anti-hepatocellular carcinoma activity and hepatotoxicity of artichoke, milk thistle and borututu. Ind Crops Prod 2013; 49:61-65.

19. Abd El-Wahab AE, Ghareeb DA, Sarhan EE, Abu-Serie MM, El Demellawy MA. In vitro biological assessment of *Berberis vulgaris* and its active constituent, berberine: antioxidants, anti-acetylcholinesterase, antidiabetic and anticancer effects. BMC complement Altern. Med 2013;13(1):218.

20. Gardin NE. Immunological response to mistletoe (*Viscum album* L.) in cancer patients: A four-case series. Phytother Res. 2009; 23:407–11. [PubMed] [Google Scholar].

21. Yener Z, Celik I, Ilhan F, Bal R. Effects of *Urtica dioica* L. seed on lipid peroxidation, antioxidants and liver pathology in aflatoxin-induced tissue injury in rats. Food Chem Toxicol 2009;47(2):418-424.

22. A. H. Arbab, M. K. Parvez, M. S. Al-Dosari et al., "Hepatoprotective and antiviral efficacy of *Acacia mellifera* leaves fractions against hepatitis B virus," BioMed Research International, vol. 2015, Article ID 929131, 10 pages, 2015.

23. Whitley NT, Day MJ. Immunomodulatory drugs and their application to the management of canine immune-mediated disease. J Small Anim Pract. 2011; 52:70–85. [PubMed] [Google Scholar].

24. H. M. ELAmin, Trees & Shrubs of the Sudan, Itaca Press, Exeter, UK, 1990.

25. A. I. Abuelgasim, H. Nuha, and A. Mohammed, "Hepatoprotective effect of *Lepidium sativum* against carbon tetrachloride induced damage in rats," Research Journal of Animal & Veterinary Sciences, vol. 3, pp. 20–23, 2008.



Available online at www.globalresearchonline.net

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

26. S. A. M. Ali, Hepatoprotective activity of aqueous extracts of *Nigella sativa* seeds and Khaya senegalensis bark in rats, Faculty of Veterinary Medicine. Khartoum University, Khartoum, Sudan, 2011, Thesis.

27. Khan TH, Sultana S. Antioxidant and hepatoprotective potential of *Aegle marmelos* Correa. against CCl4-induced oxidative stress and early tumor events. J Enzyme Inhib Med Chem 2009;24(2):320-327..

28. Bueno PR, Buno CB, Santos DL, Santiago LA. Antioxidant activity of *Ficus pseudopalma* Blanco and its cytotoxic effect on hepatocellular carcinoma and peripheral blood mononuclear cells. Curr ResBio Pharma Sci 2013; 2:14, 21.

29. Prasad KN, Xie H, Hao J, Yang B, Qiu S et al. Antioxidant and anticancer activities of 8-hydroxypsoralen isolated from wampee [*Clausena lansium* (Lour.) Skeels] peel. Food Chemis 2010;118(1):62-66.

30. Gupta M, Mazumder UK, Sambath Kumar R, Sivakumar T, Gomathi P et al. Antioxidant defense system induced by a methanol extract of *Caesalpinia bonducella*. in rat liver. Pharm Biol 2005;43(5):411-419.

31. Sivalo kanathan S, Ilayaraja M, Balasubramanian MP. Antioxidant activity of *Terminalia arjuna* bark extract on N-nitrosodiethylamine

induced hepatocellular carcinoma in rats. Mol Cell Biochem 2006;281(1-2):87.

32. Abdel-Azeem AS, Hegazy AM, Ibrahim KS, Farrag AR, effects of ginger (*Zingiber officinale* Roscoe) and vitamin E in acetaminophen treated rats. J Diet Suppl. 2013; 10(3):195209, ElSayed EM. Hepatoprotective, antioxidant, and ameliorative.

33. Pareek A, Godavarthi A, Issarani R, Nagori BP. Antioxidant and hepatoprotective activity of *Fagonia schweinfurthii* (Hadidi) Hadidi extract in carbon tetrachloride induced hepatotoxicity in HepG2 cell line and rats. J Ethnopharmacol. 2013; 150(3):973-981.

34. Sikander M, Malik S, Parveen K, Ahmad M, Yadav D, Hafeez ZB, Bansal M. Hepatoprotective effect of *Origanum vulgare* in Wistar rats against carbon tetrachloride-induced hepatotoxicity. Protoplasma. 2013; 250(2):483-493.

35. Singhal KG, Gupta GD. Hepatoprotective and antioxidant activity of methanolic extract of flowers of *Nerium oleander* against CCl4-induced liver injury in rats. Asian Pac J Trop Med. 2012; 5(9):677-685.

For any questions related to this article, please reach us at: globalresearchonline@rediffmail.com New manuscripts for publication can be submitted at: submit@globalresearchonline.net and submit_jjpsrr@rediffmail.com

