Review Article

A Review on Hepatoprotective Herbal Plants

Yash Anand Sinha*[1], Rohit Kumar Bijauliya[1], Janab Khan[1], Prashant Kumar Singh[2]
[1]BIU College of Pharmacy, Bareilly International University, Bareilly, Uttar Pradesh, India.
[2]Rameshwaram Institute of Technology and Management, Lucknow, Uttar Pradesh, India.
***Corresponding author's E-mail:** rkpharma3791@gmail.com

Received: 10-04-2022; **Revised:** 22-06-2022; **Accepted:** 28-06-2022; **Published on:** 15-07-2022.

ABSTRACT

The liver is an important organ that aids in xenobiotic metabolism and elimination. Excessive alcohol use, toxic substances (particular chemotherapeutic drugs, antibiotics, thioacetamide (TAA), carbon tetrachloride (CCl_4), and microorganisms) have all been shown to induce liver cell harm. In this scenario, the current synthetic medications to treat liver problems exacerbate liver damage. As a result, herbal medicines have grown in popularity and are widely used. Herbal remedies have long been used to treat liver problems, and maintaining a healthy liver is critical for an individual's overall health. On the market, there are a variety of herbal preparations. The goal of this study is to collect information on potential phytochemicals from medicinal plants that have been investigated in hepatotoxicity models using contemporary scientific methods.

Keywords: Medicinal plant, Liver, Hepatoprotective, Phytochemical, Hepatotoxicity.

QUICK RESPONSE CODE →

DOI: 10.47583/ijpsrr.2022.v75i01.015

DOI link: http://dx.doi.org/10.47583/ijpsrr.2022.v75i01.015

INTRODUCTION

Traditional medicines, contemporary medications, nutraceuticals, dietary supplements, folk medicines, pharmaceutical intermediates, bioactive principles, and lead compounds in synthetic pharmaceuticals all use medicinal plants as a source of innovative drugs. Plants provide primary health care for more than 80% of the world's population, according to WHO. Overexploitation of chosen medical plant species, on the other hand, resulted in a decrease in the number of plants in the wild and their names being added to the red data book [1, 2]. Nature has provided an abundance of therapeutic plants on our nation. Throughout history, plants have been employed as a traditional healing method. The WHO has identified 20,000 medicinal plants worldwide, with India accounting for 15-20% of them. [3] According to the WHO, medicinal plants are used in 80 percent of the world's countries. [4] A substantial amount of data has been gathered to demonstrate the potential of medicinal herbs employed in diverse traditional systems. Over 13 000 plants have been examined for various diseases and afflictions all over the world in the last few years. [5, 6]

Liver Diseases

The liver is the most vital organ in the body, as it is responsible for many physiological functions. It helps in metabolism, secretion, and storage, among other things. Many exogenous and endogenous chemicals are detoxified and excreted through it. As a result, any damage to it or impairment of its function has serious health consequences for the individual afflicted. Although viral infection is one of the leading causes of hepatic damage, over 18,000 people are known to die each year from liver cirrhosis induced by hepatitis. The liver's critical function in chemical clearance and transformation makes it vulnerable to drug-induced harm. [7]

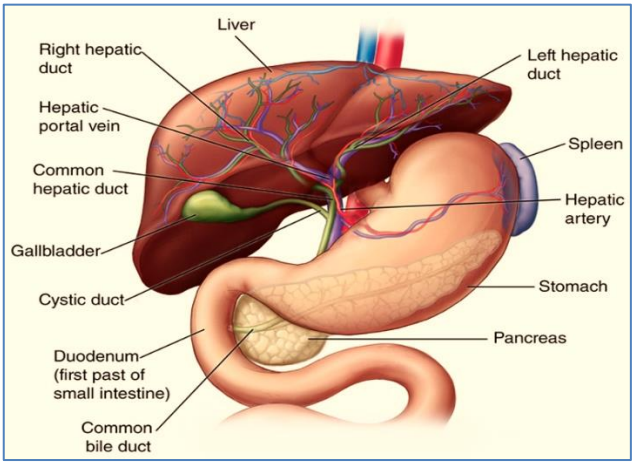

Figure 1: Structure of Liver

Liver disorders are one of the most dangerous illnesses. Acute or chronic hepatitis (inflammatory liver disorders), hepatosis (non-inflammatory diseases), and cirrhosis are the different types (degenerative disorder resulting in fibrosis of the liver). Toxic substances (particular antibiotics, chemotherapeutics, peroxidized oil, aflatoxin, carbon-tetrachloride, chlorinated hydrocarbons, etc.), excessive alcohol use, infections, and autoimmune/ disorders are the primary causes of liver disease [8].

Causes of Liver Diseases

Because of food choices, alcohol use, poor cleanliness, uncontrolled drug use, and smoking, liver problems are the most frequent health concern in underdeveloped nations. Non-inflammatory, inflammatory, and degenerative liver disorders are all possibilities. Hepatic insufficiency is linked to a higher risk of atherosclerosis and cardiovascular disease [9, 10]. Hepatotoxicity can be induced by a variety of poisons such as carbon tetrachloride (CCl_4), thioacetamide, acute or chronic alcohol intake, diseases such as hepatitis A, B, and C, and drugs, with drugs being the most prevalent culprit. Hepatitis and cirrhosis are caused by the production of free radicals caused by alcohol use[11].

Role of Medicinal Plants in Hepatotoxicity

Plant materials have been employed in Ayurveda to protect the liver from different poisons and dietary factors. As a result, herbal medications have gained popularity in recent years due to their safety and capacity to heal ailments. These drugs are also incredibly cost-effective when used for a long time. Many medicinal plants found across India have been identified as hepatoprotective medications, and they are widely utilised to treat liver problems. Hepatoprotective action is found in a variety of plants and polyherbal preparations. Hepatoprotective action has been claimed for around 160 phytoconstituents and other phytochemicals [12]. Over 87 plants are utilised in India, with 33 of them being trademarked and having exclusive multi-ingredient plant compositions [13]. The authors analysed studies on medicinal plants' hepatoprotective properties and grouped them in systematic order as indicated in table 1.

Table 1: List of Plant has Hepatoprotective Activity

Plant Name	Plant part	Extract	Active constituents	Mechanism
Allium sativum (Alliaceae)	Bulb	-	Organosulfur compounds	Prevention of GSH depletion, alteration of GSH-dependent Enzymes [14]
Azadirachta indica (Meliaceae)	Leaf	70% ethanol	Flavonoids	(Glutathione peroxidase (GPx), glutathione-S-transferase (GST), superoxide dismutase (SOD) and catalase (CAT) [15]
Arachniodes exilis (Dryopteridaceae)	Rhizomes	Ethanol	Polyphenols	Lipid peroxide, DPPH, ABTS, superoxide anion, hydroxyl radical and hydrogen peroxide, glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, malondialdehyde and superoxide dismutase [16]
Asparagus racemosus (Liliaceae)	Whole plant	purified aqueous fraction	Polysaccharides	Lipid peroxidation, protein oxidation[17]
Baliospermum montanum (Euphorbiaceae)	Roots	Alcohol, chloroform	-	SGPT, SGOT and alkaline phosphate, Histopathological changes in liver. [18]
Buddleja officinalis (Loganiaceae)	flowers and buds	-	Phenyl ethanoid Glycoside (Acteoside)	Decreased levels of AST, ALP [19]
Boerhaavia diffusa (Nyctaginaceae)	Roots	Aqueous	-	GOT, GPT, ACP and ALP, but not GLDH and bilirubin [20]
Cassia tora (Caesalpiniaceae)	Leaves	Ethyl acetate	-	Glutathione enzyme activities. [21]
Camellia sinensis (Theaceae)	Leaves	-	Polyphenols (Catechin)	Inhibited hepatocellular apoptosis and unregulated Bcl-2 protein expression [22]
Cistus laurifolius L. (Cistaceae)	Leaves	Ethanol	Flavonoid (Quercetin)	MDA, AST, GSH levels decreased[23]
Corydalis saxicola (Papaveraceae)	Whole plant	Ethanol	Alkaloid Dehydrocavidine	Decreased levels MDA, SOD, GPx [24]
Cordia macleodii (Boraginaceae)	Leaves	Ethanolic	Flavonoids and triterpenoids	Increased Glutamate pyruvate transaminase (GPT), serum glutamate oxaloacetate transaminase (GOT), Alkaline Phosphatase (ALP) and total bilirubin[25]
Cassia fistula (Leguminosae)	Leaf	Methanol	Anthraquinone and steroids	Lowering the serum levels of transaminases (SGOT and SGPT), bilirubin and alkaline phosphatase (ALP). [26]
Cochlospermum Planchoni (Coclospermaceae)	Rhizomes	Aqueous	tannins, carotenoids, flavonoids and triterpenes	Total bilirubin Alkaline phosphatase Alanine aminotransferase [27]

Eglets viscosa Less. (Asteraceae)	Whole plant	Hexane and Ethanol	Flavonoid (Ternatin)	Decreased lipid peroxidation [28]
Gardenia jasminoides (Rubiaceae)	Fruit	-	Iridoid Glycoside Geniposide	Antioxidant [29]
Ginkgo biloba L. (Ginkgoaceae)	Leaves	Petroleum ether	Polyphenols	ALT, AST, ALP, ALB, TP, HA, LN, TG, and CHO levels decreased [30]
Gossypium herbaceum (Malvaceae)	Root, leaves, stem	-	Polyphenols Gossypol	Antioxidant [31]
Hibiscus sabdariffa L. (Malvaceae)	flowers	Ethanol, chloroform	Polyphenols Protocatechuic acid	LDH, AST, ALP, MDA levels decreased [32]
Kalanchoe pinnata Pers. (Crassulaceae)	Leaves	Juice of the fresh leaves and ethanolic extract	-	Decreased Serum glutamyl oxalacetic acid transaminase (SGOT), serum glutamyl pyruvate transaminase (SGPT) alkaline phosphatase (ALKP), serum bilirubin (SBLN) [33]
Larrea tridentata (Zygophyllaceae)	Leaves	-	Resin Nordihydroguaiaretic acid	Antioxidant [34]
Magnolia officinalis (Magnoliaceae)	Bark, root, stem	-	Polyphenols Magnolol	Antioxidant [35]
Momordica dioica (Cucurbitaceae)	Leaves	Ethanolic and aqueous	-	Decreased serum glutamate oxaloacetate transaminase (AST), serum glutamate pyruvate transaminase (ALT), serum alkaline phosphatase (SALP) and total [36]
Mangifera indica (Anacardiaceae)	-	-	Triterpene (Lupeol)	Decreased levels of SGOT, SGPT, ALP, bilirubin [37]
Nigella sativa (Ranunculaceae)	-	-	Quinones Thymoquinone (TQ)	Scavenger of superoxide, hydroxyl radical, and singlet molecular oxygen [38]
Ocimum basilicum (Lamiaceae or Labiatae)	-	-	Phenolic Acids (Rosmarinic acid)	AST, ALP, SGOT levels decreased [39]
Orthosiphon stamineus (Lamiaceae)	Leaves	Methanol	-	AST, ALT and ALP [40]
Peumus boldus (Monimiaceae)	-	-	Alkaloid Boldine	Lipid peroxidation [41]
Pinus maritima (Pinaceae)	Bark	-	Polyphenols (Pycnogenol)	SOD, GSH-Px, GSH-reductase, and TBARS levels decreased [42]
Rubia cordifolia (Rubiaceae)	Roots	50% aqueous ethanolic	Glycoside (Rubiadin)	SGOT, SGPT, SALP, and gamma-GT levels decreased [43]
Schisandra chinensis (Schisandraceae)	Bee pollen	-	Lignans (Wuweizisu)	Antioxidant [44]
Sida cordifolia (Malvaceae)	Leaves	Aqueous	Organic compound (Fumaric acid)	Antioxidant [45]
Silybum marianum (Asteraceae)	-	-	Lignans (Silymarin)	Antioxidant [46]
Tridax procumbens (Asteraceae)	Leaves	Ethanolic	-	Decreased Glutathione, superoxide dismutase and catalase [47]
Vitis vinifera (Vitaceae)	Leaves	Chcl3, etoac, n-buoh, and water	Phenolic compounds	Decreased (plasma and liver tissue MDA [malondialdehyde], transaminase enzyme levels in plasma [AST-aspartate transaminase, ALT-alanine transferase] and liver GSH [glutathione] levels) [48]
Zanthoxylum armatum (Rutaceae)	Bark	Ethanolic	Isoquinoline alkaloid, berberine, as well as flavonoids and phenolic compounds,	Decreased serum transaminases, alkaline phosphatase and total bilirubin and antioxidant enzymes: superoxide dismutase, catalase and glutathione [49]

CONCLUSION

Since ancient times, herbal and traditional botanical medicines have been utilised to cure a variety of ailments and diseases. Active extracts, fractions, or a combination of fractions/extracts might prove to be extremely effective medications. For liver disorders, plant medications (combinations or single pharmaceuticals) should be effective enough to treat serious liver diseases caused by toxic chemicals, viruses (Hepatitis B, Hepatitis C, etc.), excessive alcohol use, and other factors. All forms of severe liver disorders cannot be treated with a single medicine. Effective formulations must be created utilising indigenous medicinal herbs, as well as pharmacological tests and clinical studies. Standards of safety and efficacy should regulate the manufacturing of plant products.

Acknowledgement: The authors are grateful to Mr. Rohit Kumar Bijauliya, Assistant Professor in BIU College of Pharmacy, Bareilly International University, Bareilly, India for providing the necessary laboratory facilities and we are also thankful for his valuable guidance.

REFERENCES

1. Ahmedullah M and Nayar MP: Red data book of Indian plants, (Peninsular India), Calcutta: Botanical Survey India. 1999.
2. Bijauliya RK, Alok S, Chanchal DK, Sabharwal M and Yadav RD: An updated review of pharmacological studies on *Azadirachta indica* (neem). Int J Pharm Sci & Res 2018; 9(7): 2645-55. doi: 10.13040/IJPSR.0975-8232.9(7).2645-55.
3. Gupta R and Chadha KL: Medicinal and aromatic plants in India. In: Gupta R, Chadha KL, editors. Advances in horticulture: medicinal and aromatic plants. New Delhi: Malhotra Publishing House; 1995, p. 44.
4. Pareek SK: Medicinal plants in India: Present status and future prospects. In: Prospects of medicinal plants. New Delhi: Indian Society for Plant Genetic Resources NBPGR Campus; 1996, p. 14.
5. Dahanukar A, Kulkarni RA, Rege NN: Pharmacology of medicinal and natural products. Indian J Pharmacol 2000; 32: 81-118.
6. Bijauliya RK, Alok S, Jain SK Singh VK, Singh D and Singh M: Herbal and allopathic medicine for kidney, gallbladder and urinary stones: a review. Int J Pharm Sci Res 2017; 8(5): 1935-52.doi: 10.13040/IJPSR.0975-8232.8(5).1935-52.
7. Ilyas U, Katare DP, Aeri V, Naseef PP: A review on hepatoprotective and immunomodulatory herbal plants. Phcog Rev 2016; 10: 66-70.
8. Kumar CH, Ramesh A, Suresh Kumar JN, And Ishaq BM: A review on hepatoprotective activity of medicinal plants. International Journal of Pharmaceutical Sciences and Research. 2011; 2(3): 501-515.
9. Dominiczak MH: Lipids, lipoproteins In: Baynes JW, Dominiczak MH (eds.) Medical biochemistry, Elsevier Mosby. Philadelphia 2005; 234-242
10. Ekaidem IS, Akpan HD, Usoh IF, Etim OE, Ebong PE: Effects of Ethanolic Extract of *Azadirachta indica* Leaves on Lipid Peroxidation and Serum Lipids of Diabetic Wistar Rats. Acta Biological Szegedensis 2007; 51: 17-20.
11. Anand K and Lal UR: Hepatitis and medicinal plants: An Review 2016; 5: 408-415.
12. Jannu V, Baddam PG, Boorgula AK, Jambula SR: A review on hepatoprotective plants. Inter J Drug Development Res 2012; 4 : 1-8.
13. Handa SS, Sharma A, Chakarborty KK: Natural Products and plants as liver protecting drugs. Fitoterapia 1986; 57: 307-51.
14. Sabayan B, Foroughinia F, Chohedry A: A postulated role of garlic organosulfur compounds in prevention of valproic acid hepatotoxicity. Med Hypotheses 2007; 68: 512-4.
15. Chattopadhyay RR and Bandyopadhyay M: Possible Mechanism of Hepatoprotective Activity of *Azadirachta indica* Leaf Extract Against Paracetamol-Induced Hepatic Damage In Rats: Part III, Indian J Pharmacol, June 2005; 37: 184-185.
16. Zhoua BD, Ruana J, Caia Y, Xionga Z, Weifua, Weia A: anti-antioxidant And Hepatoprotective Activity of Ethanol Extract of *Arachniodes exilis* (Hance) Ching, Journal of Ethanopharmacology 2010; 129: 232–237.
17. Jayashree P, Kamat A, Krutin K, Boloor A, Thomas PA, Devasagayam A, Venkatachalam B: antioxidant Properties of *Asparagus racemosus* against Damage Induced By G-Radiation in Rat Liver Mitochondria, Journal of Ethnopharmacology 2000; 71: 425–435.
18. Wadekar RR, Supale RS, Tewari KM, Patil KS, Jalalpure SS: Screening of Roots of *Baliospermum montanum* for Hepatoprotective Activity Against Paracetamol *Induced* Liver Damage In Albino Rats, International Journal Of Green Pharmacy, 2010; 220-223.
19. Lee KJ, Woo ER, Choi CY, Shin DW, Lee DG, You HJ. Protective effect of acteoside on carbon tetrachloride-induced hepatotoxicity. Life Sci 2004; 74: 1051-64.
20. Rawat KS, Mehrotra AS, Tripathi SC and Shome BU: Hepatoprotective Activity of *Boerhaavia diffusa* L. Roots - A Popular Indian Ethnomedicine, Journal Of Ethnopharmacology 1997; 56: 61- 66.
21. Dhanasekarana M, Ignacimuthua S, Paulagastianb, Potential Hepatoprotective Activity of Ononitol Monohydrate Isolated from *Cassia tora* L. On Carbon tetrachloride Induced Hepatotoxicity In Wistar Rats, Phytomedicine 2009; 16: 891–895.
22. Xu C, Shu WQ, Qiu ZQ, Chen JA, Zhao Q, Cao J: Protective effects of green tea polyphenols against subacute hepatotoxicity induced by microcystin-LR in mice. Environ Toxicol Pharmacol 2007; 24 :140-8.
23. Kupeli E, Orhan DD, Yesilada E. Effect of *Cistus laurifolius* L. leaf extracts and flavonoids on acetaminophen-induced hepatotoxicity in mice. J Ethnopharmacol 2006; 103: 455-60.
24. Wang T, Sun NL, Zhang WD, Li HL, Lu GC, Yuan BJ: Protective effects of dehydrocavidine on carbon tetrachloride-induced acute hepatotoxicity in rats. J Ethnopharmaco 2008; 117: 300-8.

25. Naseem N, Qureshi A, Bhanudansh S, Kuchekar B, Nadeem A, Logade A, Majid A. Haleem A, Antioxidant And Hepatoprotective Activity of *Cordia macleodii* Leaves, Saudi Pharmaceutical Journal, 2009; 17: 299– 302.

26. Bhakta T. A et al., Evaluation of Hepatoprotective Activity of Cassia Fistula Leaf Extract, Journal of Ethnopharmacology 1999; 66: 277–282.

27. Roseline Aliyu A, Okoye ZSC, Thomas Shier B: The Hepatoprotective Cytochrome P-450 Enzyme Inhibitor Isolated From The Nigerian Medicinal plant *Cochlospermum planchonii* Is A Zinc Salt, Journal Of Ethnopharmacology 1995; 48: 89-97.

28. Souza MF, Rao VS, Silveira ER: Prevention of acetaminophen-induced hepatotoxicity by ternatin, a bioflavonoid from *Egletes viscosa* less. Phytother Res 1998; 12: 557-61.

29. Tseng TH, Chu CY, Huang JM, Shiow SJ, Wang CJ: Crocetin protects against oxidative damage in rat primary hepatocytes. Cancer Lett 1995;97:61-7.

30. Yang L, Wang CZ, Ye JZ, Li HT. Hepatoprotective effects of polyprenols from Ginkgo biloba L. leaves on CCl_4-induced hepatotoxicity in rats. Fitoterapia 2011; 82: 834-40.

31. Randel RD, Chase CC Jr, Wyse SJ: Effects of gossypol and cottonseed products on reproduction of mammals. J Anim Sci 1992; 70: 1628-38.

32. Tseng TH, Hsu JD, Lo MH, Chu CY, Chou FP, Huang CL. Inhibitory effect of *Hibiscus protocatechuic* acid on tumor promotion in mouse skin. Cancer Lett 1998; 126: 199-207.

33. Yadav NP and Dixit VK: Hepatoprotective Activity of Leaves of *Kalanchoe pinnata* Pers, Journal of Ethnopharmacology 2003; 86: 197–202.

34. Arteaga S, Andrade-Cetto A, Cardenas R. *Larrea tridentata* (Creosote bush), an abundant plant of Mexican and US-American deserts and its metabolite nordihydroguaiaretic acid. J Ethnopharmacol 2005; 98: 231-9.

35. Lin YR, Chen HH, Ko CH, Chan MH: Neuroprotective activity of honokiol and magnolol in cerebellar granule cell damage. Eur J Pharmacol 2006; 537: 64-9.

36. Jain A, Soni M, Deb L, Jain A, Roult AP, Gupta VB, Krishna KL: Antioxidant and Hepatoprotective Activity of Ethanolic and Aqueous Extracts of *Momordica dioica* Roxb. Leaves, Journal of Ethnopharmacology 2008; 115: 61–66.

37. Kumari A and Kakkar P: Lupeol prevents acetaminophen-induced *in vivo* hepatotoxicity by altering the Bax/Bcl-2 and oxidative stress-mediated mitochondrial signalling cascade. Life Sci 2012; 90: 561-70.

38. Abdel-Wahab WM: Protective effect of thymoquinone on sodium fluoride-induced hepatotoxicity and oxidative stress in rats. J Basic Appl Zoo 2013; 66: 263-70.

39. Liu Y, Flynn TJ, Ferguson MS, Hoagland EM: Use of the Combination Index to determine interactions between plant-derived phenolic acids on hepatotoxicity endpoints in human and rat hepatoma cells. Phytomedicine 2013; 20: 461-8.

40. Chin JH, Hussin AH And Ismai :, Anti-Hepatotoxicity Effect of Orthosiphon Stamineus Benth Against Acetaminophen-Induced Liver Injury In Rats By Enhancing Hepatic GST Activity, Pharmacognosy Research, March-April 2009; 1: 53-58.

41. Lanhers MC, Joyeux M, Soulimani R, Fleurentin J, Sayag M, Mortier F: Hepatoprotective and anti-inflammatory effects of a traditional medicinal plant of Chile, Peumus boldus. Planta Med 1991 ;57: 110-5.

42. Yang YS, Ahn TH, Lee JC, Moon CJ, Kim SH, Jun W: Protective effects of pycnogenol on carbon tetrachloride-induced hepatotoxicity in Sprague-Dawley rats. Food Chem Toxicol 2008; 46: 380-7.

43. Rao GM, Rao CV, Pushpangadan P, Shirwaikar A: Hepatoprotective effects of rubiadin, a major constituent of Rubia cordifolia Linn. J Ethnopharmacol 2006; 103: 484-90.

44. Cheng N, Ren N, Gao H, Lei X, Zheng J, Cao W: Antioxidant and hepatoprotective effects of Schisandra chinensis pollen extract on CCl_4-induced acute liver damage in mice. Food Chem Toxicol 2013; 55: 234-40.

45. Silva RL, Melo GB, Melo VA, Antoniolli AR, Michellone PR, Zucoloto S: Effect of the aqueous extract of *Sida cordifolia* on liver regeneration after partial hepatectomy. Acta Cir Bras 2006; 21(Suppl 1): 37-9.

46. Upadhyay G, Kumar A, Singh MP: Effect of silymarin on pyrogallol- and rifampicin-induced hepatotoxicity in mouse. Eur J Pharmacol 2007; 565: 190-201.

47. Reddipalli H: Anti-Hepatotoxic and Anti-Oxidant Defense Potential of Tridax Procumbens, International Journal of Green Pharmacy, 2010; 164-169

48. Didem DO, Nil¨Ufer O, Ender E, Fatma E: Hepatoprotective Effect of *Vitis vinifera* L. Leaves on Carbontetrachloride-Induced Acute Liver Damage In Rats, Journal of Ethnopharmacology 2007; 112: 145–151.

49. Singh L, Ranawat, Bhatt J, Paetl J, Hepatoprotective activity of Ethanolic Extracts of Bark of *Zanthoxylum armatum* DC In CCl_4 Induced Hepatic Damage in Rats, Journal of Ethnopharmacology 2010; 127: 777–780.

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.