Multiple approach of natural hepatoprotectant against chemical toxicity

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World Journal of Biology Pharmacy and Health Sciences, 2022, 11(03), 157–166

Publication history: Received on 15 August 2022; revised on 02 October 2022; accepted on 05 October 2022

Article DOI: https://doi.org/10.30574/wjbphs.2022.11.3.0148

Abstract

Plants are the major source of various ingredients which are responsible for the treatment of diseases and complications. They are used from ancient times mentioned in the Ayurveda and various Vedas because herbal medicine and their products are safe, very effective and environmental eco-friendly. They are less toxic and easily available. On the other hand, liver is the major vital organ performing major functions in the body like detoxification, biotransformation etc. It synthesizes proteins and produces biochemical’s necessary for digestion and growth. Its other roles in metabolism include the regulation of glycogen storage, decomposition of red blood cells and the production of hormones. In spite of this environment pollutants or toxicants accumulate in the liver and causes ill effects on liver. They change the architecture of hepatocytes and diminished the functions of liver due to this reason metabolism of the body changes. Hence there is urgent need to some liver tonic. Considering all these facts present review article explored the natural hepatoprotectant against chemical toxicity.

Keywords: Hepatoprotectant; Rat; Chemicals; Multiple approach; Liver

1. Introduction

As soon as the human race marches towards 21st century the problem of environment pollution also becomes grave and of utmost concern globally. The use of toxic chemicals, certain synthetic compounds such as pesticides, urea and various types of metallic compounds can not be denied. Metallic compounds have been playing a major role in almost all kinds of pollution. It reaches the environment after its releases by industries making various types product. The released compounds in the environment may be bioconcentrated and thus enter the food chain. Food water and air are the main medium through which we are constantly exposed to various metallic compounds which finally accumulate in the liver and produced liver toxicity. For minimization of liver toxicity, the use of herbal drug could be of immense global importance as the adverse effects of synthetic compounds on health status may be responsible for varied types of complicated diseases. Management of hepatic disorders have becomes a matter of serious concern worldwide and several laboratories are engaged in identifying effective hepatoprotectant from different sources using different experimental models [78].

In the light of present understanding about the role of hepatoprotectant against chemicals deformities, this article provides an account of multifaceted activities of hepatoprotective activity due to which these phytocehmicals deserve proper position in therapeutic armamentarium.

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2. Hepatoprotection against chemicals

Rana et al. studied the hepatoprotective activity of Gymnema sylvestre and Curcuma zedoaria against CCl₄ toxicity. Both plants have been claimed to be useful in liver ailments. It was considered worthwhile to evaluate the efficacy of their alcoholic extracts in preventing damage induced by CCl₄ with the help of morphological, biochemical and functional parameters [70]. Chandan et al. demonstrated hepatoprotective activity of alcoholic extract of whole plant Boerhaavia diffusa against carbon tetrachloride induced hepatotoxicity in rats and found an increase in normal bile flow in rats suggesting a strong choleretic activity [13]. Rana and Avadhoot worked on Gymnema sylvestre and Curcuma zedoaria in rats against hepatotoxicity of carbon tetrachloride and achieved significant changes in biochemical parameters, liver weight and liver volume affected by carbon tetra chloride [69]. Shukla et al. performed hepatoprotective activity of ursolic acid isolated from Eucalyptus hybrid against paracetamol and galactosamine induced hepatotoxicity in rats with reference to hepatoprotective drug, Silymarin [89]. Bishayee and Chatterjee estimated carrot aqueous extract protection against hepatic oxidative stress and lipid peroxidation induced by acute carbon tetrachloride intoxication in mice [10].

Vinsen et al. observed prevention of galactosamine induced hepatic damage by Picroliv on isolated hepatocytes [98]. Saraf et al. assessed anti-hepatotoxic activity of Cassia occidentalis against carbon tetrachloride in rats [76]. Jafari et al. reported hepatoprotective activity of leaves of Cassia occidentalis against paracetamol and ethyl alcohol intoxication in rats [34]. Singh and Handa demonstrated hepatoprotective activity of Apium graveolens and Hygrophiia auriculata against paracetamol and thioacetamide intoxication in rats with the normalcy of all raised enzymatic profile [82]. Kamiyama et al. demonstrated effects of one year cadmium exposure on hepatorenal and their relation to glutathione level [42]. Saraswat et al. revealed protective action of ursolic acid against chemical induced hepatotoxicity in rats [77]. Vaidya et al. investigated Picrorhiza kurroa as a hepatoprotectant against galactosamine induced liver injury in rats. Picrorhiza kurroa restored reduction in liver lipid content, AST and ALT affected by galactosamine induction [95]. Kataria and Singh demonstrated hepatoprotective effect of Liv-52 and Kumaryasava on carbon tetrachloride induced hepatic damage in rats. Kumaryasava to be more effective in reducing the liver weight increased due to hepatotoxicity of carbon tetrachloride [45]. Churungoo et al. overviewed Silymarin mediated differential modulation to toxicity induced by carbon tetrachloride, paracetamol and D-galactosamine in freshly isolated rat hepatocytes [16]. Mitra and Sur estimated hepatoprotective activity with Glycosmis pentaphylla leaves and stem bark extract against hepatic injury by carbon tetrachloride in albino rats [57]. Mukherjee et al. observed hepatoprotective effect of Swertia chirata against intraperitoneal injection of carbon tetrachloride in albino rats [58]. Chin-Chuan Tsai et al. evaluated four prescriptions of traditional Chinese medicine: Syh-Mo-Ylin Guizhi-Fuling-Wan, Shieh-Qing-wan and Syh-Nih-Sann on experimental acute liver damage in rats [15]. Suja et al. established protective effect of Liv-52 and Liv-100, ayurvedic formulations on lipid peroxidation in rat liver homogenate. The protective effect of drugs is attributed to the enhanced supply of reduced glutathione that inhibit the deleterious process of lipid peroxidation [88]. Kanase et al. attained curative effects of Mandur bhasma on liver and kidney of albino rats after induction of acute hepatitis by carbon tetrachloride [43]. Mitra et al. evaluated hepatoprotective activity of aqueous extract of bark and leaves of Glycosmis pentaphylla against CCl₄ toxicity at dose rate of 750 mg/kg body wt. The therapeutic dose range was devoid of toxic effects [57]. Mukherjee et al. observed hepatoprotective activity of aqueous extract of Swertia chirata against CCl₄ toxicity at moderate dose i.e. 50 mg/kg body wt. [58].

Despande et al. described protective effects of turmeric (Curcuma longa) extract on carbon tetrachloride induced liver damage in rats [19]. Subramoniam et al. worked on hepatoprotective activity of Trichopus zeylanicus extract against paracetamol induced hepatic damage in rats. Induced hepatotoxicity was judged from the serum marker enzymes, liver histology and level of lipid peroxidation in liver [87]. Dutta et al. evaluated hepatoprotective effect of a protein isolated from Cajanus indicus (Spreng) on carbon tetrachloride induced hepatotoxicity in mice [20]. Despande et al. exhibited protective effect of Curcuma longa alcoholic extract on carbon tetrachloride induced liver damage in rats. The results indicate that turmeric is a hepatoprotective agent in vivo on liver cells [19]. Subramoniam et al. carried out hepatoprotective activity of Trichopus zeylanicus aqueous as well as methanolic extract against paracetamol induced hepatic damage in rats. Its methanolic extract (100 mg/ kg body wt.) showed a remarkable hepatoprotective activity and judged from the serum marker enzymes, liver histology and levels of lipid peroxides in liver [87].

Singh et al. assessed hepatoprotective activity of ellagic acid against carbon tetrachloride induced hepatotoxicity in rats [83]. Sandhir and Gill found hepatoprotective effects of Liv-52 on ethanol induced liver damage in rats [75]. Janbaz and Gilani studied preventive and curative effects of berberine on chemical induced hepatotoxicity in rodents and confirmed the pre and post treatment of berberine (4 mg/kg b.wt.) was hepatoprotective in action [36]. Prabakan et al. described protective effects of Hemidesmus indicus against rifampicin and isoniazid induced hepatotoxicity in rats [66]. Huel et al. isolated hepatoprotective effects of Solanum alatum on acetaminophen induced hepatotoxicity in mice. The hepatoprotective mechanism may function through direct binding with acetaminophen toxic metabolites [31]. Prabakan et al. enlighten protective effect of ethanolic extract of Hemidesmus indicus against rifampicin and isoniazid.
induced hepatotoxicity in rats. The results suggest that the dose 100 mg/kg body wt. for 15 was sufficient to best recovery [66]. Trivedi and Rawal demonstrated hepatoprotective and antioxidant properties of aqueous extract of *Andrographis paniculata* in BHC induced liver damage in mice. The study clearly indicates that the antioxidant effect elucidated by aqueous extract of *Andrographis paniculata* is possibly due to their ability to activate antioxidant enzymes that catalyse the reaction of oxidants [92]. Sreepriya and Devaki attained effect of methanolic extract of *Indigofera tinctoria* on liver antioxidant defense system during D-galactosamine/ endotoxin induced hepatitis in rodents. The results of the present study indicate that pretreatment with *Indigofera tinctoria* extract improves hepatic enzymic and non enzymic antioxidant status [86].

Attri conducted experiment with protective effect of N-acetylcysteine (NAC) in isoniazid induced hepatic injury (INH) in growing rats. The supplementation of NAC with INH protected the animals against hepatotoxic reactions by minimizing the free radical induced tissue injury [6] Buwa et al. established hepatoprotective action of Abharak bhasma an ayurvedic drug in albino rats against hepatitis induced by carbon tetrachloride [12]. Trivedi and Rawal attained hepatoprotective and antioxidant property of *Andrographis paniculata* (Nees) in BHC induced liver damage in mice. Nees prevents the increased activity of enzyme glutathione-s-transferase and lipid peroxidation [92]. Emmanuel et al. made hepatoprotective effect of coumestans isolated from the leaves of *Wedelia calendulacea* in paracetamol induced liver damage [24]. Asha performed preliminary studies on the hepatoprotective activity of *Mamordica subangulata* and *Naragamia alata* against paracetamol induced hepatotoxicity in rats [5]. Hukkeri et al. studied hepatoprotective activity of *Ailanthus excelsa* leaves extract on experimental liver damage in rats. In the biochemical parameter of reduction in the elevated enzyme levels of serum ALT, AST and ALP was determined as a criterion their hepatoprotective activity [33]. Kapoor et al. exhibited hepatoprotective activity of *Nigella sativa* against paracetamol induced hepatotoxicity in rats [44]. El-Khatib et al. reported prophylactic effect of aqueous *Propolis* extract against acute experimental hepatotoxicity in vivo and found decrease in lactate dehydrogenase (LDH), lipid peroxide and glutathione content [23]. Pari reported hepatoprotective activity of *Moringa oleifera* on anti-tubercular drug induced liver damage in rats [64]. Abdel- Wahhab and Ahmed suggested protective effect of Korean *Panax ginseng* against chromium VI toxicity and free radicals generation in rats. Korean *Panax ginseng* exhibited a protective action against the toxic effect of chromium VI and it had the ability to scavenge free radicals resulted from chromium VI intoxication [1].

Kamat et al. enlighten hepatoprotective activity of leaves of *Feronia elephantum* (Rutaceae) against carbon tetrachloride induced liver damage in rats [41]. Rao et al. examined hepatoprotective effect of *Coccinia indica* against carbon tetrachloride hepatotoxicity in rats. Hepatic damage as evidenced by a rise in the levels of AST, ALT, ALP and GGT in serum and also change observed in other biochemical parameters in serum and liver showed a tendency to attain near normalness in animals co-administered with extract [71]. Hukkeri et al. conducted hepatoprotective activity of stem bark of *Butea monosperma* (Kunzte) in carbon tetrachloride treated rats. The extract exhibited a positive hepatoprotective activity by decreasing the levels of biochemical parameters assessed, like serum AST, ALT and ALP [33]. Janbaz et al. investigated hepatoprotective activity of thymol against paracetamol and carbon tetrachloride induced hepatic damage in rodents [37]. Velanganni and Balasundaram examined protective effect of vitamin A, ascorbic acid and alpha-tocopherol on 2, 4-dimethyl amino benzene induced hepatoma in rats. Oral administration of antioxidant vitamins has a protective effect on the incidence of liver tumor monitored on the basis of liver weight, histological studies and enzymatic analysis [96]. Al-Howiriny et al. made preliminary evaluation of the anti-inflammatory and anti-histotoxic activity of *Parsley* *Petroselinum crispum* in rats [2]. Ulcina et al. studied hepatoprotective effect of *Aspalathus linearis* (Rooibos tea) on carbon tetrachloride induced liver damage in rats. The anti-fibrotic effect in the experimental model of hepatic cirrhosis of rats suggests the use of rooibos tea as a plant hepatoprotector in the diet of patients with hepatopathies [94]. Kale et al. observed the effect of aqueous extract of *Azadirachta indica* leaves on hepatotoxicity induced by anti-tubercular drugs in rats [40]. Shukla et al. revealed effect of propolis extract on acute carbon tetrachloride induced hepatotoxicity. The propolis extracts exhibited recoupment in both pre and post treatment of biochemical changes induced by carbon tetrachloride [81]. Biswas and Khuda-Bukhsh carried out evaluation of protective potentials of a potentialized homeopathic drug, *Chelidonium majus*, during azo dye induced hepatocarcinogenesis in mice [11]. Venukumar and Lalha observed hepatoprotective effect of *Coscinium fenestratum* in rats following carbon tetrachloride intoxication [97].

Patil et al. attained hepatoprotective activity of aqueous extract of leaves of *Feronia elephantum* against thioacetamide and allyl alcohol intoxication in rats [65]. Zaman and Ahmad evaluated hepatoprotective effects of *Raphanus sativus* on rabbits. The anti-inflammatory and anti-apoptosis activity of *Raphanas sativus* may be responsible for this hepatoprotective activity [100]. Ozbek et al. reported hepatoprotective effect of *Foeniculum vulgare* essential oil: a carbon tetrachloride induced liver fibrosis model in rats [63]. Hewawasam et al. described hepatoprotective effect of *Epaltes divaricata* extract on carbon tetrachloride induced hepatotoxicity in mice [31]. Johri et al. carried out analysis of time dependent recovery from beryllium toxicity following chelation therapy and antioxidant supplementation [39]. Deger et al. reported effects of *Nigella sativa* and vitamin E+Se in carbon tetrachloride treated rats. The administration
of vitamin E+ Se and Nigella sativa have a positive effect against hepatic damage by carbon tetra chloride [18]. Gao et al. reported hepatoprotective activity of chloroform extract of Terminalia catappa leaves on carbon tetra chloride induced acute liver damage and D-galactosamine induced hepatoocyte injury [28]. Kumar and Kumar studied protective effects of vitamin C against copper poisoning with special reference to the liver of rat [46]. Luo et al. studied reversing effect of Ginkgo biloba extract on established carbon tetra chloride induced liver fibrosis in rats [50]. Al-Qarawi et al. investigated protective effect of Phoenix dactylifera on carbon tetra chloride induced hepatotoxicity in rat’s results revealed that treatment with aqueous extract significantly reduced carbon tetra chloride induced elevation in plasma enzyme and bilirubin concentration and ameliorated morphological and histological liver damage in rats [3]. Rukkumani et al. studied hepatoprotective activity of Feulic acid against alcohol in albino rats [73].

Bayram et al. described hepatoprotective effect of pentoxifylline against carbon tetrachloride toxicity in male Sprague Dawley rats [8]. Kumar et al. examined Spirulina fusiformis: a food supplement against mercury induced hepatic toxicity in Swiss albino rats. The Spirulina fusiformis extract orally before and after mercury intoxication showed a significant decrease in lipid per oxidation level, AST and ALT activity and increase in serum alkaline phosphatase activity and GSH content in spite of mercuric chloride [47]. Mukherjee et al. evaluated aqueous extract of black tea (Camellia sinensis) against chronic ethanol toxicity [58]. Sozmen et al. conducted to investigate vitamin C or kefir protected Swiss albino mice against azoxymethane toxicity [85]. Tabassum et al. found hepatoprotective studies on Phyllanthus niruri on paracetamol induced liver cell damage in albino mice [90]. Maheshwari and Rao observed anti-hepatotoxic effect of grape seed oil in albino rats [52]. Rathore and Varghese exhibited effect of mercuric chloride on survival, food intake, body weight, histological and haematological changes in mice and their prevention with Liv-52 [72]. Gajawat et al. studied to screen for the hepatoprotective role of ascorbic acid against lead acetate intoxication in mice. The ascorbic acid treatment prior to lead intoxication reduced the depletion in the normal hepatocytes count and elevation in bi-nucleated as well as abnormal hepatocytes in comparison to their respective control [26]. Nair described protective effect of Tefrol-a polyherbal mixture on cadmium chloride induced hepatotoxic rats [60]. Saxena and Mahour evaluated Panax ginseng as hepatoprotectant against mercuric chloride intoxicated albino rats [78]. Sharma et al. demonstrated the protective effect of Mentha piperita against arsenic induced toxicity in liver of Swiss albino mice [80]. Gill et al. reported the role of phytocelaltion in phytoremediation of heavy metals [29].

Naik et al. found the hepatoprotective effect of ginkgoslect phytosome in rifampicin induced liver injury in rats [59]. Gopal and Sengottuvelu performed hepatoprotective activity of Clerodendrum inerma against carbon tetra chloride induced injury in rats [30]. Hsin-Yi Peng et al. exhibited hepatoprotector of Chlorella against carbon tetra chloride induced oxidative damage in rats [32]. Udoka E. Obioka et al. evaluated hepatoprotective potentials of onion and garlic extracts on cadmium induced oxidative damage in rats [93]. Chandrashekhar et al. studied hepatoprotective activity of Stereospermum suaveolens against carbon tetra chloride induced liver damage in albino rats [14]. Rana et al. deliberated hepatoprotection by carotenoids in isoniazid rifampicin induced hepatic injury in rats [68]. Alshawsh et al. demonstrated hepatoprotective effects of Orthosiphon stamineus extract on thioacetamide induced liver cirrhosis in rats [4]. Lin et al. conducted hepatoprotection in rat model of acute liver damage through inhibition of CY2E1 activity by total alkaloids extracted from Rubus alcefolius Poir. [48]. Teraoka et al. observed molecular mechanisms of the hepatoprotective effect of goswin A against oxidative stress and inflammatory response in rats with carbon tetra chloride induced acute liver injury [91]. Eidi et al. examined hepatoprotective activity of Cinnamomn ethanol extract against carbon tetra chloride induced liver injury in rats [22]. Xia et al. described hepatoprotective activity of pueraarin against carbon tetrachloride induced injuries in rats [99]. Ganie et al. reported hepatoprotective and antioxidant activity of rhizome of Podophyllum hexandrum against carbon tetra chloride induced hepatotoxicity in rats [27]. Omidi et al. investigated hepatoprotective effect of Crocus sativus (saffron) petals extract against acetaminophen toxicity in male wistar rats [62]. Senthilkumar et al. evaluated hepatoprotective effect of Rhodiola imbricate rhizome against paracetamol induced liver toxicity in rats [79].

Jaiswal et al. found hepatoprotective effect of citrus Limon fruit extract against carbofuran induced toxicity in wistar rats [35]. Soulj et al. performed hepatoprotective effect of carob against acute ethanol induced oxidative stress in rat [84]. Sadeghi et al. exhibited hepatoprotective effect of Rosa canina fruit extract against carbon tetra chloride induced hepatotoxicity in rat [74]. Jiang et al. demonstrated hepatoprotective and antioxidant effects of lycopene on non alcoholic fatty liver disease in rat [38]. Lin et al. established hepatoprotective activities of rosmarinic acid against extra hepatic cholestasis in rats [49]. Mahmodzadeh et al. experimented on rats for the hepatoprotective effect of methanolic Tanacetum partHENHGEN extract on carbon tetra chloride induced liver damage in rats [53]. Das et al. studied hepatoprotective effects of green capsicum annuum against ethanol induced oxidative stress inflammation and apoptosis in rats [17]. Mehrzadi et al. recognized hepatoprotective effect of berberine against methotrexate induced liver toxicity in rats [56]. Ebtams et al. evaluated assessment of the hepatoprotective effect of developed lipid polymer hybrid nanoparticles encapsulating naturally extractd B-sitosterol against carbon tetra chloride induced hepatotoxicity in rats [21]. Azarmehr et al. reported hepatoprotective and antioxidant activity of watercress extract on acetaminophen
induced hepatotoxicity in rats [7]. Mahaldar et al. performed antioxidant and hepatoprotective activity of Piper retrofrctum against paracetamol induced hepatotoxicity in Sprague dawley rat [51]. Binitha et al. described hepatoprotective effect of Lobelia alsinoides Lam. in wistar rats [9]. Naji et al. attained hepatoprotective activity of velittin on isoniazid and rifampicin induced liver injury in male albino rats [61]. Farid et al. deliberated anti inflammatory, antioxidant and hepatoprotective effects of Lactoferrin in rats [25].

3. Conclusion

Plants have been used from ancient times as ointment and drugs for various diseases. They are safe, eco-friendly and very cheap. On the other hand, chemicals are very dangerous to human as well as animals and causing severe toxicity. Hence an attempt has been taken as multiple approach of natural hepatoprotectant against chemical toxicity. Form the above research it is clear that the natural Hepatoprotectant is very helpful in liver toxicity in comparison to synthetic Hepatoprotectant.

Compliance with ethical standards

Acknowledgments

The author is very thankful to late Professor P. N. Saxena, Head of department of Zoology, Dean School of life Sciences, Khandari Campus, Dr. B. R. A. University, Agra for providing me necessary facility for conducting my research work. The author follow the all the rule or regulation of ethics.

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