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Multiple approach of natural hepato-protectant against chemical toxicity

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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 CCl_4 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 CCl_4 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]. Jafri *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 *Hygrophila auriculata* against paracetamol and thioacetamide intoxication in rats with the normalency of all raised enzymatic profile [82]. Kamiyama *et al.* demonstrated effects of one year cadmium exposure on hepato-renal 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]. Chrungoo *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-Yiin 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 CCl_4 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 CCl_4 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 a*l. 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 catalyses 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-acteylcysteine (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 Abhrak 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* (Ruteaceae) 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* (Kuntze) 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 azo-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-hepatotoxic activity of 'Parsley' *Petroselinum crispum* in rats [2]. Ulicna *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 *Raphanas 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 hepatocyte 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]. Maheswari and Rao observed anti-hepatotoxic effect of grape seed oil in albino rats [52]. Rathore and Varghase 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 Tefroli-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 phytochelation in phytoremediation of heavy metals [29].

Naik *et al*. found the hepatoprotective effect of ginkoslect phytosome in rifampicin induced liver injury in rats [59]. Gopal and Sengottuvelu performed hepatoprotective activity of *Clerolendrum inerma* against carbon tetra chloride induced injury in rats [30]. Hsin-Yi Peng *et al*. exhibited hepatoprotection of Chlorella against carbon tetra chloride induced oxidative damage in rats [32]. Udoka E. Obioha *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 isoniazed 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 alceifolius Poir* [48]. Teraoka *et al*. observed molecular mechanisms of the hepatoprotective effect of gowisin 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 *Cinnamon* ethanolic extract against carbon tetra chloride induced liver injury in rats [22]. Xia *et al*. described hepatoprotective activity of puerarin 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]. Souli *et al*. performed hepatoprotective effect of carob against acute ethanol induced oxidative stress in rat [84]. Sadeghi *et a*l. 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]. Mahmoodzadeh *et al*. experimented on rats for the hepatoprotective effect of methanolic *Tanacetum parthenium* extract on carbon tetra chloride induced liver damage in rats [53]. Das *et al*. studied hepatoprotective effects of green capsicum annum 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]. Ebtsam *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 a*l. described hepatoprotective effect of *Lobelia alsinoides* Lam. in wistar rats [9]. Naji *et al.* attained hepatoprotective activity of velittin on isoniazed 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

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