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REVIEW ARTICLE

Protective Effects of Herbal Agents Against Hepatorenal Toxicity: A Review

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Abstract

Hepatorenal toxicity, characterised by damage to the liver and kidneys due to toxins, chemicals or drugs, poses a significant threat to human health. The intricate metabolic and pathophysiological connection between these vital organs underscores the urgency of effective therapeutic strategies. This article reviews various herbal interventions with their potential hepatorenal protective effects. The discussion encompasses diverse plants, each possessing unique bioactive compounds and mechanisms of action in hepatorenal toxicity. This article focuses on 14 entities including *Rheum turkestanicum, Curcuma longa, Olea europaea, Euryops arabicus, Taraxacum syriacum, Andrographis paniculata,* Grape seed oil*, Bridelia ferruginea, Cynara scolymus, Phyllanthus amarus, Schisandra chinensis, Garcinia kola* Heckle*, Cyperus laevigatus* and *Alchemilla vulgaris*. These are examined for their potential to mitigate hepatorenal toxicity. Antioxidant and anti-inflammatory activities contribute to the hepatorenal protective effects of these plants. This article also explores the combination of N-Acetyl Cysteine (NAC) with plants such as Lycopene, Curcumin and Taurine, emphasising synergistic effects in ameliorating toxic insults to the liver and kidneys. Therefore, these findings underscore the potential of plant-based interventions as promising candidates for therapeutic strategies against hepatorenal toxicity, offering a holistic approach by mitigating oxidative stress and inflammatory responses in these vital organs.

Keywords: Cirrhosis, Hepatorenal Toxicity, Inflammatory Response, Oxidative Stress, Pathophysiology, Phytochemicals

1. Introduction

Hepatorenal toxicity in general terms means damage to the kidney and liver by toxins, chemicals or drugs. The liver and kidneys are crucial organs involved in metabolism, excretion, as well as detoxification of administered substances. These organs are intricately connected in terms of both metabolism and pathophysiological connection between the kidneys and the liver[1]. The main reason for this harmful condition is a rise in Reactive Oxygen Species (ROS), resulting in oxidative stress and damage to organs. Interaction of heavy metals with cellular components increases levels of apoptotic, oxidative stress and inflammatory cytokines[2]. Following lead and arsenic, mercury (Hg) stands as the third most dangerous heavy metal. Its toxic nature gives rise to adverse clinical and physiological impacts, presenting significant health risks[3]. In addition, extended utilisation of medications, including antitubercular agents, anticancers as well as analgesics and antipyretics has been identified as a potential contributor to hepatorenal toxicity[4]. Hepatorenal toxicity may arise from various mechanisms, including the transformation of medications into hazardous intermediate metabolites,

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as observed with substances like paracetamol. Renal Replacement Therapy (RRT) serves as an interim intervention, ultimately culminating in Orthotopic Liver Transplantation (OLT) or Simultaneous Liver and Kidney Transplantation (SLK) as the conclusive therapeutic approach in both toxicities[5]. In traditional medicine, a range of ailments has historically been addressed in the management of hepatorenal toxicity using natural and herbal remedies. Many people gravitate towards herbal remedies, drawn by the allure of fewer side effects, a diminished risk of adverse drug reactions and a perception of lower hazards when contrasted with traditional medication treatments[6]. Embracing the modern shift towards herbal remedies, scientists now harness the power of specific phytoconstituents for treatment and explore the wonders of nature's pharmacy with potent herbal allies such as *C. longa, R. turkestanicum, O. europaea, E. arabicus, T. syriacum* and many others[7]. Bursting with coumarins, diterpenoids, triterpenoids, steroids, alkaloids, flavonoids and more, these botanical marvels hold immense potential in combatting hepatorenal toxicity. Their remarkable ability to diminish oxidative stress, quell inflammation, bolster antioxidant defences and foster cellular regeneration needs to be experienced[8]. Nature's bounty offers healing solutions that dazzle the senses and invigorate the spirit. Therefore, in this review, some of the best hepatorenal protective plants are discussed along with their physical characteristics and mechanisms of action. These are used because they are cheaper, have fewer side effects and have a higher level of safety than conventional medications.

2. Methodology

A systematic research for relevant scientific literature spanning the period from 2011 to 2022 was done for this study. Literature was searched on Google Scholar/ PubMed using the keywords "hepatorenal toxicity", "cirrhosis", "hepatotoxicity", "renal toxicity", "pathophysiology", "hepatorenal protective plants" etc. These terms were searched in combination with the conducted literature search by medical subject headings or Emtree terms, and free text terms. The language was restricted and only papers published in English were considered. Finally, more than 100 review papers were screened and 70 were selected for the review paper.

3. Pathophysiology of Drug-induced Hepatorenal Toxicity

The pathophysiology of drugs or chemical-induced hepatorenal toxicity involves multiple pathways, including the direct destruction of liver and kidney tissue, stimulation of pro-inflammatory cytokines, oxidative stress and impaired liver and kidney functions, apoptosis and necrosis, by triggering immune response in both organs[9-11] (Figure 1).

4. List of Hepatorenal Protective Plants

4.1 *Rheum turkestanicum*

Rheum turkestanicum belongs to the Polygonaceae family. Traditionally, the root of *R. turkestanicum*

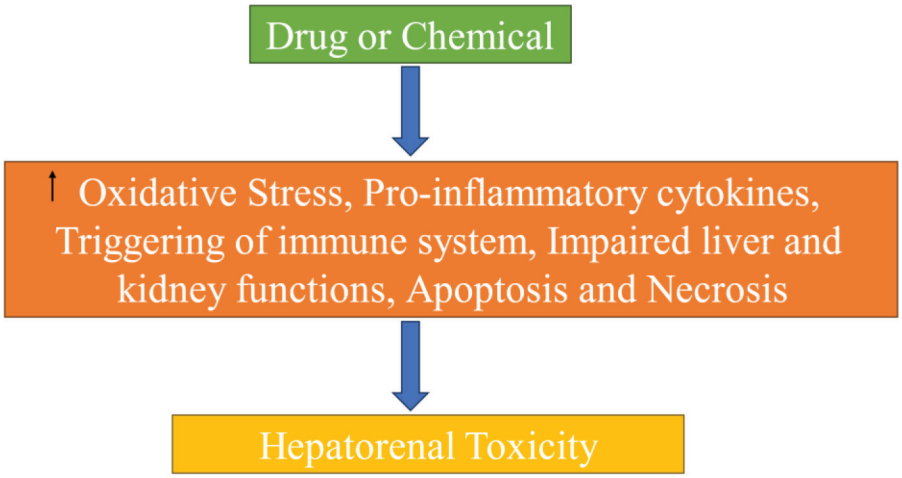

Figure 1. Pathophysiology of hepatorenal toxicity.

has been employed for addressing conditions such as diabetes, jaundice, cancer and high blood pressure[12]. It possesses potent antioxidant characteristics and might safeguard the kidneys and liver by reducing Malondialdehyde (MDA) levels and increasing thiol levels. The primary phytoconstituent found in R. turkestanicum consists of anthraquinone derivatives, notably emodin, aloe-emodin, rhein, chrysophanol, physcion and danthron. Additionally, it also contains dianthrones, stilbenes, anthocyanins, flavonoids, anthraglycosides, polyphenols, essential oils, organic acids and chromone glycosides. Hosseinni *et al*., demonstrated that extract from *R. turkestanicum* shields the liver and kidneys from toxicity induced by mercuric chloride in male Wistar rats. The safeguarding impact of the extract can be ascribed to the antioxidant properties, leading to the reduction of MDA and an increase in thiol levels. Other studies have indicated that Emodin has the potential to mitigate ischemia/reperfusion injury during kidney transplantation, possibly by diminishing lipid peroxidation and suppressing the release of inflammatory agents in which toxicity was induced by cisplatin[13].

4.2 *Curcuma longa*

Curcuma longa belongs to the family of Zingiberaceae. It is extensively utilised as a culinary spice and is also employed in traditional medicine to address various medical conditions. Curcumin is the primary phytoconstituent of *C. longa*, Due to its ability to affect numerous signalling molecules at the cellular level, it is utilised in addressing various health concerns such as motor disorders, pain, reproductive diseases metabolic syndrome, and inflammation[14,15]. Abubakar *et al*., demonstrated that the administration of *C. longa* extract or curcumin could potentially function as a promising hepatorenal protective agent in lead-induced hepatorenal toxicity in Sprague-Dawley rats. Curcumin treatment provides a defence against free radicals and reinstates both antioxidant enzymes and functional markers. A particular issue related to human exposure to mercury is the necessity for efficient treatment to manage its toxicity[16].

4.3 *Olea europea*

Olea europaea or the olive tree, is indigenous to the Mediterranean region. The existence of notable antioxidants and phenolic elements, including oleuropein, tyrosol, and hydroxytyrosol, serves to hinder oxidative harm. In addition, the olive leaf encompasses various compounds, including rutin, vanillin, verbascosid, p-coumaric acid, vanillic acid, luteolin and caffeic acid. These components exhibit a range of pharmacologically advantageous properties, such as cytotoxicity against human breast cancer cells, inhibition of blood cancer cell multiplication, antiarrhythmic effects, hypotensive effects, anti-HIV effects and antimalarial effects[17,18]. It is thought that olive oil offers physiological advantages primarily due to its antioxidant activity. While the composition of olive oil is intricate, the main categories of components believed to contribute to its noted health benefits are squalene, phenolics and oleic acid. These constituents have demonstrated efficacy in reducing oxidative stress and providing protective effects for the liver and kidneys[19]. Maalej *et al*. explored the preventative impact of ethanolic extract from Olive Fruit Extract (OFE) and its phenolic compound, Oleuropein (OLE), in mitigating hepatorenal damage triggered by Deltamethrin (DEM) in male Wistar rats. Both treatments reduced the expression of p53 and increased the levels of bcl-2. The protective effect was mediated by their free radical scavenging properties by scavenging DPPH free radical and ABTS activities. The presence of polyphenolic compounds, particularly catechol groups, is responsible for the antioxidant activity (rutin, luteolin, hydroxytyrosol, verbascoside, oleuropein)[20].

4.4 *Euryops arabicus*

Euryops arabicus resides in the family Asteraceae, broadly used in the southwestern region as a traditional herbal to address various ailments such as pain, inflammation and skin injuries. It has been noted that *E. arabicus* possesses essential oils, terpenoids and flavonoids. Furthermore, *E. arabicus* exhibits free radical scavenging properties and antibacterial, anti-inflammatory and hepatoprotective characteristics[21]. Hafez *et al*., concluded that *E. arabicus* possesses the capacity to shield the liver and kidneys from the harmful impacts of acetaminophen by stimulating the endogenous antioxidant defence system using male albino rats. Flavonoids also possess anti-inflammatory activity by decreasing the entry of cellular inflammation and rejuvenation of hepatocytes near the central vein. *E. arabicus* has been proven to enhance the expression of

the rate-limiting enzyme in the synthesis of γ-glutamyl cysteine synthetase, leading to a simultaneous rise in intracellular glutathione concentrations due to flavonoids. Volatile oil from *E. arabicus* also exhibited hepatorenal protective activity[22,23].

4.5 *Taraxacum syriacum*

Taraxacum syriacum (TS) or dandelion is part of the family Asteraceae. In traditional medicine, it has been utilised for its choleretic, laxative, diuretic, anti-inflammatory properties and antirheumatic. Additionally, it is employed in the treatment of jaundice, skin ailments, anaemia, Gastrointestinal (GI) disorders and vision problems. Eshrati *et al.*, highlighted the remarkable potential of TS extract as a candidate for alleviating Acetaminophen (APAP)-induced hepatorenal toxicity in Wistar rats of male gender. The ethanolic TS root extract exhibits a dose-dependent effect against APAP, preventing destructive cascades caused by free radicals and suppressing inflammatory processes by modulating Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB), inhibiting the expression of cyclooxygenase-2 and restraining the production of Tumour Necrosis factor (TNF-α) and Interleukin (IL)-1[24]. The antioxidant properties of this plant are linked to its phenolic, flavonoid and coumaric acid constituents, which exhibit potent reducing power and the ability to scavenge superoxide, peroxide, peroxynitrite and hydroxy, showcasing significant antioxidant potential[25].

4.6 *Andrographis paniculata*

Andrographis paniculata is a herbaceous plant with roots in traditional herbal practices and falls within the family of Acanthaceae[26]. Several bioactive compounds were identified in *A. paniculata* leaves including 14-deoxy andrographolide and 14-deoxy-11,12-didehydroandrographolide, andrographolide, deoxygrapholide quercetin, kaempferol and apigenin using Gas Chromatography (GC)[27]. Previous research found that key compounds in *A. paniculata*'s methanolic extract, including andrographolide, 14-deoxy-11,12-didehydroandrographolide and 14-deoxy andrographolide, can counteract arsenic-induced toxicity. This may occur by neutralising excess free radicals or boosting the antioxidant defence system through the extract[28]. Owoade *et al.*, showcased the remarkable potential of *A. paniculata* extract in alleviating arsenic-induced hepatorenal toxicity in male Wistar rats. Their findings suggest that the extract's ability to neutralise excessive free radicals and halt the toxicity cascade may lie in its rich content of bioactive compounds, particularly flavonoids and terpenoids[29].

4.7 Grape Seed Oil

Grape (*Vitis vinifera*) is a widely consumed fruit, because of the nutritional and pharmaceutical properties of its derivatives. Derived from the winemaking process, Grape Seed Oil (GSO) is utilised as a cooking oil due to its elevated levels of phenolic compounds, fatty acids, phytosterols and vitamins. Polyphenols consist of flavonoids like catechin, epicatechin, procyanidin (with potent antioxidant properties against free radicals and oxidative stress), anthocyanidin, phenolic acids like gallic acid and ellagic acid and stilbenes such as resveratrol and piceid. Flavonoids exhibit antioxidant effects by counteracting hydroxyl radicals and superoxide[30]. According to available data, GSO has powerful anti-inflammatory, free radical scavenging properties, and antineoplastic effects[31]. Ahmed *et al.*, unveiled the remarkable protective prowess of grape seed oil (GSO) against ivermectin-induced hepatorenal toxicity in female mice. Remarkably, pretreatment with GSO three weeks prior to ivermectin intoxication restored serum liver and kidney biochemical parameters to normal levels, accompanied by notable improvements in renal histological morphology. These beneficial effects were attributed to the polyphenolic compounds present in GSO, renowned for their potent free radical scavenging properties[32,33].

4.8 *Bridelia ferruginea*

Bridelia ferruginea Benth. (Euphorbiaceae) is a woody bush. Phytochemical constituents consist of eugenol, pyrogallol, sitosterol, Vanillyl Methyl Ketone, phytol acetate, podophyllotoxin, stigmasterol, 2-coumaranone, isovanillic acid, cymene, Phytosol, 4-phenyl benzophenone, petroselinic acid, stigmasta-3,5-dien-7-one, lupeol, β and α-amyrin acetate, and vitamin E acetate[34]. Oloyede *et al.*, unveiled the remarkable capability of the aqueous extract derived from the stem bark of *B. ferruginea* in combating Cd-induced hepatorenal toxicity in Wistar rats. Renowned

for its antioxidant prowess, *B. ferruginea* emerges as a beacon of hope, effectively mitigating oxidative stress and inflammation within the liver and kidneys. Administered to groups exposed to cadmium, the aqueous extract exhibited significant reductions in serum activities of Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP) and Aspartate Aminotransferase (AST) while concurrently enhancing total protein proportion compared to both untreated cadmium-induced hepatorenal toxicity and normal control groups. Moreover, the extract demonstrated the ability to bolster hepatic and renal antioxidant parameters, serum lipid profiles, urea and creatinine levels. Notably, a marked decrease in renal and hepatic cadmium concentrations was observed in groups that received the extract, accompanied by histological evidence showcasing the restoration of normal tissue architecture in the kidneys and liver of Wistar rats[35].

4.9 *Cynara scolymus*

The artichoke *(Cynara scolymus)* belonging to Asteraceae is recognised as a nutritious food containing minerals, proteins and a substantial amount of phenolic compounds and flavonoids. The artichoke has been shown to safeguard against body nexus damage caused by oxidative stress and to replenish the anti-oxidant system in instances of toxicity due to lead, metabolic diseases and hepatotoxicity triggered by the antifungal drug fluconazole, respectively[36].

Al *et al.*, explored the defensive effects of Artichoke Leaf Extract (ALE) in opposition to Cd-induced hepatorenal toxicity in Wistar rats. ALE treatment demonstrated a multifaceted impact, reducing oxidative stress damage, immunosuppression and haematological disturbances while improving hepatic and renal markers. It significantly enhanced the antioxidant system and decreased. The abundance of flavonoids in artichoke contributed to its potent antioxidant properties, effectively reducing ROS. Furthermore, the study emphasised the presence of entire phenolic constituents, caffeic acid and chlorogenic acid in artichoke, along with its impressive ROS scavenging capacity. Remarkably, artichoke supplementation not only fortified the antioxidant system but also served as a protective barrier against free radical formation and lipid peroxidation. The flavonoids in artichoke played a crucial role in reducing immunosuppressive cytokines such as TNF-α and IL-6 while boosting IL-10 levels[37].

4.10 *Phyllanthus amarus*

*Phyllanthus amarus (*Phyllanthaceae) is commonly used for the treatment of hepatic and renal disorders, asthma, constipation and many others[38]. Olabiyi *et al.*, delved into the hepatoprotective and nephroprotective effects of *P. amarus* (PA) extract against streptozotocin-induced damage in male Wistar rats. Their findings unveiled the remarkable ability of PA leaf extract to shield the liver from oxidative damage, potentially by decreasing lipoperoxidation rates and improving the free radical scavenging defence mechanism. The suggested mechanism primarily revolves around the phytochemical lignan - phyllanthin, which exhibits antioxidant effects against the oxidative damage induced by hepatotoxins. Moreover, *P. amarus* demonstrated nephroprotective activity, possibly attributed to its antioxidant properties. This research illuminates the promising therapeutic potential of *P. amarus* extract in safeguarding liver health, offering a compelling narrative in the realm of natural remedies[39].

4.11 *Schisandra chinensis*

Schisandra chinensis belongs to the Schisandraceae family and is recognised for its medicinal properties. *Schisandra* lignans exhibit diverse pharmacological effects, including anti-HIV, cytotoxic, antioxidant and anti-inflammatory activities. Additionally, certain Schisandra nortriterpenoids display potential biological activities such as anti-HIV properties and cytotoxicity[40].

Researchers from China identified that *S. chinensis* Fructus (SCF) exhibits hepatoprotective and enzyme-reducing characteristics, with SCF lignans acting as the main active constituents. This includes Schisandrin A, Schisandrin B, Schisandrol A and Schisandrol B[41]. Wei *et al.*, reveal the protective abilities of *S. chinensis* extract against cyclosporin A hepatorenal toxicity in rats. This notable outcome is accomplished by activating the Nuclear Factor Erythroid 2-related Factor (Nrf2) signalling pathway and restraining apoptosis. Extracts of *S. chinensis* demonstrate the ability to hinder the formation and buildup of oxygen-free radicals within tissues, thereby mitigating oxidative damage and safeguarding against liver injury. Additionally, they suppress the activation of the Jun N terminal Kinase (JNK) signalling pathway and control the B-cell lymphoma 2 (Bcl-2)/Bax signalling is employed to

inhibit apoptosis of hepatocyte and depress caspase cleavage. Furthermore, these extracts enhance the antioxidant condition of mitochondrial function in the kidneys[42-44].

4.12 *Garcinia kola* Heckel

Garcinia kola Heckel belongs to the family of Clusiaceae. In Nigeria, *G. kola* seeds are frequently enjoyed as a refreshing snack with significant medicinal properties, believed to contribute to longevity. Kolaviron, an extract derived from these seeds, has demonstrated efficacy in ameliorating hepatorenal toxicity induced by antituberculosis drugs through the suppression of inflammatory reactions and reduced the elevated malondialdehyde level, improved biochemical (ALT, AST, GSH, LPO)[45]. The presence of specific polyphenols like lupeol, tirucallol, β-amyrin, etc., Human Gingival Epithelium Keratinocytes (HEGK) may be associated with the exhibited biological activities[46]. In compelling research done by Folayana *et al*. The impact of the hexane extract derived from *G. kola* seeds Heckel on hepatorenal toxicity induced by cisplatin in male Balb/c mice was thoroughly investigated. The results showcased a notable reduction in GSH and MDA content in both the hepatic and renal, indicating a potential protective effect. This safeguarding mechanism may be credited to the diminution of elevated MDA levels as well increment of Biochemical and antioxidant markers in the kidney and liver tissues of mice. The extract not only demonstrated its protective prowess but also played a crucial role in restoring the cytoarchitecture. This included the mitigation of hepatic tissue necrosis, alleviation of widespread congestion in renal interstitial vessels, and suppression of hyperplasia of the stellate sinusoidal macrophages[47].

4.13 *Cyperus laevigatus*

Cyperus plant by-products exhibited considerable biological and pharmacological potential. *Cyperus laevigatus* was found to predominantly contain derivatives of luteolin and tricin. The flavonoids identified in this plant extract exhibit strong abilities to scavenge free radicals, which are credited to the presence of multiple hydroxyl groups in their aromatic structures. Specifically, hydroxylation at the 3′ and 4′ positions of the B ring, as well as at the 5 positions of the A ring, along with the presence of a carbonyl group at the 4 positions, enhance the antioxidant and anti-inflammatory characteristics. These properties aid in shielding against oxidative stress, stabilising cellular membranes and suppressing inflammatory cytokines[48]. Luteolin derivatives, particularly methoxylated derivatives and glycosides, play a particular role in anti-inflammatory and free radical scavenging actions, offering protection against liver and kidney injuries[49-51]. Phenolic acids like quinic acids, caffeic, cinnamic and ferulic function as active metabolites, playing a crucial role in safeguarding the hepatic and renal. They achieve this by neutralising free radicals, preventing liver cholestasis, activating Adenosine Monophosphate (AMP)-activated protein kinase or mitogen-activated protein kinase, reducing inflammatory cytokines in the kidneys, improving the kidney's oxidative status and reducing lipoperoxidation[52,53].

4.14 *Alchemilla vulgaris* L

Alchemilla vulgaris L is a part of the Rosaceae family and is popularly recognised as Lady's mantle. The presence of a substantial quantity of tannins, flavonoids phenolic acids and other phenolic compounds in *A. vulgaris* contributed to its observed biological activity[54]. Juric *et al*., showcased the protective effects of *A. vulgaris* extracts against cisplatin-induced hepatorenal toxicity in male Wistar rats. *A. vulgaris* demonstrated a reduction in renal Thiobarbituric Acid Reactive Substances (TBARS) levels and an improvement in certain biochemical parameters associated with kidney damage. Additionally, it maintained the levels of most hepatic serum parameters close to normal values. High levels of phenolics were detected in the aerial components of *A. vulgaris*, particularly ellagic acid, which endows it with a wide range of activities, including hepatoprotection and nephroprotection. Ellagic acid also played a role in suppressing the levels of most serum biochemical parameters related to liver injury. Moreover, it exhibited the ability to inhibit lipoperoxidation and showed antioxidant activity, indicating its potential to counteract free radicals within cellular structures (Table 1)[55].

Table 1. List of herbal plants with hepatorenal protective activity

S. No.	Plant	Phytochemicals	Protective Activity	References
1	*Rheum turkestanicum*	Emodin, Flavonoids	Antioxidant activity	13
2	*Curcuma longa*	Curcumin	Chelating activity and inhibition of oxidative stress	16
3	*Olea europea*	Phenolic compound, Oleuropein	Decreased p53 expression and upregulated bcl-2 levels	20
4	*Euryops arabicus*	Flavonoids	↑Expression c- glutamylcysteine synthetase and intracellular glutathione concentrations	22,23
5	*Taraxacum syriacum*	Carvacrol, phenolic polyphenol and Coumaric acid	Antioxidant, anti-inflammatory and anti peroxidant potential	25
6	*Andrographis paniculate*	Flavonoids and Terpenoids	Antioxidant activity, enhanced caspase-3 and TNF expressions	28,29
7	*Vitis vinifera*	Polyphenolic	Free radicals' scavenging properties	32,33
8	*Bridelia ferruginea*	Flavanoid	Antioxidant activity	35
9	*Cynara scolymus*	Flavonoid, Caffeic acid, Chlorogenic acid	↓ Immunosuppressive cytokines and antioxidant activity	37
10	*Phyllanthus niruri*	Lignan- phyllanthin	Antioxidant activity	39
11	*Schisandra chinensis*	Polysaccharides	Activate Nrf2 signalling pathway and the inhibition of apoptosis, JNK signalling	43,44
12	*Garcinia kola*	Lupeol, Tirucallol, b-amyrin	Antioxidant and anti-inflammatory	47
13	*Cyperus laevigatus*	Ferulic, caffeic, cinnamic, Luteolin and quinic acids	Antioxidant and anti-inflammatory.	52,53
14	*Alchemilla vulgaris*	Ellagic acid	Antioxidant activity	55

5. Combination of Plants Phytoconstituents with N-Acetyl Cysteine

NAC is a well-known antioxidant that has proven effective in disrupting disulphide linkages in various models, both *in vitro* and *in vivo*[56]. NAC is a medicinal and dietary supplement frequently employed as a mucolytic agent for addressing acetaminophen overdose[57]. NAC serves as a pro-drug of L-cysteine, a precursor pivotal to the synthesis of GSH. NAC plays a regulatory role in cellular GSH levels, thereby modulating the balance between oxidants and antioxidants. This modulation includes the inhibition of lipid peroxidation and the scavenging of ROS[58]. The metabolism of NAC into L-cysteine, a glutathione precursor, augments the glutathione-S-transferase activity. As a result, NAC facilitates detoxification and shields against the deleterious impact of free radical species, predominantly through scavenging actions and elevating the cellular concentration of free glutathione. Given its robust antioxidant characteristics, NAC presents itself as a plausible therapeutic option for conditions linked to the generation of harmful free radicals[59]. The following plants exhibiting hepatorenal protection in combination with NAC are discussed here.

5.1 Lycopene

Lycopene (LP) is an unsaturated carotenoid, derived from vitamin A, showcasing robust and effective capabilities in scavenging free radicals. Additionally, it demonstrates antibiotic, anti-inflammatory, immunostimulant and anti-mutagenic effects[60]. LP, a naturally occurring antioxidant found in tomatoes, demonstrates effectiveness against various tissue injuries mediated by oxidative stress, reducing damage to lipids, proteins and DNA caused by oxidation[61]. Elsayed *et al.*, in 2021 investigated the protective effect of LP and NAC against cisplatin-induced hepatorenal toxicity in Wistar albino rats. The combination exhibited hepatoprotective effects by reinstating the activities of Superoxide Dismutase (SOD) and Catalase (CAT), as well as the levels of GSH[62].

5.2 Curcumin

Curcumin (CUM) is a yellow compound extracted from the root tubers of *Curcuma longa*, traditionally utilised as both a food colouring agent and a preservative[63]. Recognised for its robust anti-inflammatory, anti-cancer and antioxidant properties, it is currently undergoing preclinical trials for cancer prevention[64]. Researchers have also documented the hepatoprotective, nephroprotective and radioprotective properties of curcumin[65]. El-Maddawy *et al.*, demonstrated the effect of curcumin and NAC in alleviating lead-induced hepatorenal toxicity through experimentation on male Sprague Dawley rats. The findings indicated that CUM and NAC demonstrate robust antioxidant effects by neutralising free radicals, enhancing CAT enzyme activity and elevating cellular GSH levels. This protection extends to mitigating lipid peroxidation and supporting either the stabilisation of cellular membranes or the regeneration of impaired cells[66].

5.3 Taurine

Taurine is typically absent in plant-based foods, although red algae might be an exception[67]. Taurine (2-aminoethanesulfonic acid; TAU) represents the predominant sulfur-containing amino acid freely present intracellularly in various cells and tissues[68]. TAU serves as a cytoprotective compound engaging in diverse activities such as energy synthesis, neuromodulation, calcium balance, and osmoregulation. These various functions collectively contribute to its antioxidant properties[69]. Owumi *et al.*, observed the effect of TAU and NAC against fipronil using male Wistar rats. The cytoprotective effects of TAU involve processes such as detoxification, osmoregulation, maintenance of cell membrane stability, cholesterol excretion, suppression of inflammation, oxidation regulation, fibrogenesis modulation and apoptosis control Similarly, NAC and TAU have demonstrated protective effects against organ damage caused by various chemicals. It is proposed that the combined use of NAC and TAU yielded synergistic effects, surpassing the level of protection offered by each substance individually. These results align with prior research indicating enhanced protection against various chemical-induced toxicities when both substances are administered together, as observed in previous publications[70].

6. Conclusion

In conclusion, our exploration takes a deep dive into the intricate pathophysiology of hepatorenal toxicity, unravelling the complex interplay of factors that contribute to this health concern. As we navigate through the labyrinth of physiological connections between the liver and kidneys, the spotlight shifts to a botanical symphony that showcases the remarkable effects of certain plants on mitigating hepatorenal toxicity. This article not only sheds light on diverse herbal interventions with potent hepatorenal protective effects but also unveils an exciting frontier - the synergistic dance between NAC and phytoconstituents. This dynamic combination emerges as a powerful ally against hepatorenal toxicity, offering a harmonious interplay that could revolutionise therapeutic strategies. In further exploration, it becomes evident that these highlighted plants offer just a glimpse into the vast potential of botanical interventions against hepatorenal toxicity. By broadening the scope and delving into additional botanical sources, new avenues for therapeutic intervention can be unlocked and enhance knowledge of effective strategies against hepatorenal toxicity.

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