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Herbal Interventions for Drug-Induced Nephrotoxicity: An Overview of *Pedalium murex* Linn and *Hygrophilla auriculata*

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ABSTRACT: Drug-induced nephrotoxicity, a common adverse effect of numerous medications, poses a significant challenge to healthcare providers and patients. Traditional herbal interventions have gained attention as potential therapeutic strategies for mitigating drug-induced nephrotoxicity due to their natural properties and minimal side effects. However, despite their promise, incorporating herbal remedies into conventional treatments presents challenges in terms of standardization, dosage determination, and potential herb-drug interactions. This review article provides an overview of two herbal remedies, *Pedalium murex* Linn and *Hygrophilla auriculata*, which have shown promising nephroprotective effects. *Pedalium murex* Linn, commonly known as 'Gokhru', has been traditionally used in Ayurvedic medicine for its diuretic, anti-inflammatory, and antioxidant properties. Experimental studies have demonstrated its ability to attenuate drug-induced renal damage, protect against oxidative stress, and reduce inflammation markers in animal models. *Hygrophilla auriculata*, also known as 'Kokilaksha', is another herb with potential nephroprotective properties. It possesses antioxidant, anti-inflammatory, and anti-apoptotic effects, which have been shown to prevent drug-induced renal injury and preserve renal function in preclinical studies. The contributions of this review lie in the compilation and critical analysis of scientific evidence on the beneficial effects of *Pedalium murex* Linn and *Hygrophilla auriculata* in drug-induced nephrotoxicity. Furthermore, the review discusses the underlying mechanisms of action of these herbal remedies, shedding light on the pathways through which they exert their nephroprotective effects. The challenges associated with integrating herbal interventions into mainstream healthcare are also discussed, emphasizing the importance of further research to establish standardized protocols and assess potential interactions with conventional medications. Overall, this review provides valuable insights into the potential of these herbal remedies as adjunct treatments for drug-induced nephrotoxicity, while highlighting the need for cautious and evidence-based implementation in clinical practice.

Keywords: Drug-induced nephrotoxicity, Herbal interventions, *Pedalium murex* Linn, *Hygrophilla auriculata*, Nephroprotective effects.

INTRODUCTION

The kidneys are vital organs responsible for filtering waste and toxins from the bloodstream. However, drug-induced nephrotoxicity (DIN) can cause damage to these organs and lead to serious health consequences. DIN is a common problem in clinical practice, and it is caused by various drugs such as antibiotics, analgesics, chemotherapy agents, and immunosuppressive agents. It is crucial to identify and manage DIN in a timely manner to avoid permanent kidney damage and renal failure. Currently, treatment options for DIN include discontinuation of the offending agent, hydration therapy, and supportive care to manage symptoms and maintain kidney function. However, these treatments have limitations, and there is a need for more effective and targeted therapeutic interventions. In recent years, there has been increasing interest in natural products and herbal remedies for the prevention and treatment of DIN (Al-Naimi *et al*., 2019).

The current state of healthcare has led to an increase in the incidence of diseases, adverse drug reactions, and therapeutic failures. Consequently, there is a pressing need to explore new or additional sources of medicine to address these issues. Among the most promising areas to look for new medications are herbs. These natural products have been found to contain numerous drugs that can be used as pharmacotherapeutic agents to treat a variety of illnesses and adverse occurrences. In fact, according to the World Health Organization, traditional plant-based medicines represent the major source of healthcare for more than 80% of the world's

population, particularly in both developing and developed nations (World Health Organization, 2019). In the quest for better healthcare, natural remedies like herbs, nutritional supplements, vitamins, minerals, and trace elements, as well as traditional and complementary therapies, have been extensively used. The use of natural items in healthcare has been shown to improve the physical condition of patients (Cohen & Hunter 2017). Natural Products (NPs) are selected based on their inherent biological relevance, which is linked to their favored molecular structures and their role in carrying out specific biological tasks in the context of signaling cascades and protein interactions (Bai & Wang 2017). NPs have a diverse range of functional groups, pharmacophores, and a strong stereochemical component, which can explain their diverse potentials through complex mechanisms that influence different pathways and result in their therapeutic effects (Li & Lou 2018). Herbal medicine (HM) offers a balance between complementary and alternative therapies. It has gained acceptance across the globe and is increasingly integrated into significant healthcare systems (Bent, 2008). In fact, the increasing demand for herbal medicine has led to an annual global market sales increase to nearly $62 billion (Bodeker *et al.*, 2007). This growth in patronage and use is driven by the importance of natural products, which are known for their low toxicity, efficacy in treating difficult ailments, flexibility in availability, preparation, and use (Barrett *et al.*, 1999). Most biologically active natural ingredients used in HM preparations are derived from plants or herbs, although some formulations may include ingredients like mushrooms and bee products, minerals (kaolin, bentonite), ashes, clams, insects, and animal parts. However, some of these ingredients may have negative effects. Therefore, the use of pharmaceuticals and herbal remedies should be appropriate and properly regulated to avoid mistreatment and misconceptions. The effectiveness of herbal medicines as medical tools is primarily dependent on their toxic side effects. However, there is a knowledge gap among doctors, pharmacists, nurses, and the public from health workers, which has contributed to misconceptions and drawbacks associated with the use of herbal medicines, particularly regarding their benefits. Thus, it is crucial to have adequate and ample knowledge about herbal medicine, particularly on crucial subjects like advantages, efficacy, safety, and toxicity, as well as on topics like formulation, research and development, legislation, analytical methods, quality control, and economic significance. The abundance of natural herbs and plants presents an exciting opportunity to discover novel chemical constituents that can be harnessed to combat the devastating effects of nephrotoxicity. The present study delves into the exploration of two potent plants, *Pedalium murex* Linn. and *Hygrophila auriculata*, which are widely found in various regions of India. These plants possess remarkable pharmacological properties that have been shown to be efficacious in ameliorating nephrotoxicity induced by various drugs, including Paracetamol, Cisplatin, and Gentamycin. *Pedalium murex*, a member of the Pedaliaceae family, is a ubiquitous plant that is found across the globe, including India, tropical Africa, Sri Lanka, Pakistan, and Mexico. Its versatility is matched only by its efficacy, as it has been shown to possess abundant quantities of sapogenin (diosgenin-0.06%), soluble proteins, and flavonoids. In fact, cold-water extracts of its various components have been found to be highly effective in treating urinary system disorders, such as gonorrhea, dysuria, and urinary incontinence. Additionally, the Ayurvedic system of medicine has long recognized its potent tonic, aphrodisiac, appetizer, and anti-inflammatory properties, which make it an asset in treating a host of ailments ranging from strep throat to bladder stones. *Hygrophila auriculata*, a member of the Indian Acanthaceae family, is another plant that has been extensively studied for its therapeutic potential. Literature suggests that it is widely distributed across India's tropical and subtropical regions and has been traditionally used for treating dysentery, asthma, cancer, and tubercular fistula. The root, leaf, and seeds of this plant have shown remarkable efficacy in treating inflammatory conditions such as jaundice, hepatic congestion, urinary infections, gout, edema, and diabetes, as well as bacterial infections. The promising pharmacological properties of these two plants make them valuable targets for further research in the fight against nephrotoxicity. By unlocking their full potential, we can potentially improve the lives of millions suffering from this debilitating condition. This article aims to provide a comprehensive review of the use of two herbs, *Pedalium murex* Linn and *Hygrophilla auriculata*, in the treatment of drug-induced nephrotoxicity, a serious and common adverse effect of numerous medications.

PATHWAYS INVOLVED IN DRUG INDUCED NEPHROTOXICITY

Drug-induced nephrotoxicity is a complex and multifactorial phenomenon that involves several pathways and mechanisms. These mechanisms include crystal nephropathy, apoptosis, renal tubular toxicity, glomerular injury, thrombotic microangiopathy, and inflammation, among others. The kidney plays a crucial role in maintaining a steady glomerular filtration rate (GFR) by controlling the pressures in the efferent and afferent arterioles, which are regulated by renal prostaglandin and angiotensin I. Therefore, prostaglandin inhibitors including angiotensin receptor blockers (ARBs), angiotensin-converting enzyme inhibitors (ACEIs), and nonsteroidal anti-inflammatory medications (NSAIDs) can lead to glomerular dysfunction (Lucas *et al.*, 2018). Drug-induced nephrotoxicity can be caused by cumulative dose-dependent toxicity or dose-independent toxicity at any point during treatment. Kidney damage can occur in a variety of renal compartments during the drug elimination process, including the glomerulus, the tubule endothelium, the collecting ducts, and the renal vasculature (Lindeman, 1990; Schetz *et al*., 2005). In general, several processes, such as inflammation, altered glomerular hemodynamics, crystal nephropathy, tubular cell toxicity, thrombotic microangiopathy, and

rhabdomyolysis, can account for the damage in various kidney compartments. The proximal tubule (PTC) epithelial cells are a primary target for nephrotoxic agents due to their functions inglomerular filtrate concentration, drug distribution, and biotransformation. Despite significant use, certain medications have been shown to cause renal damage, PTC damage, and other systemic toxicity (Morrissey *et al.,* 2013). Essential medicines such as Paracetamol (PCM), Gentamycin (GM), Cisplatin (Cis), and heavy metals such as lead, mercury, and arsenic, can cause severe nephrotoxicity with long-term usage (Schetz *et al.,* 2005). In this experiment, we focus on three of these drugs, Paracetamol, Cisplatin, and Gentamycin, which are the most common causes of drug-induced nephrotoxicity. Drug-induced nephrotoxicity can also be caused by altered renal intraglomerular hemodynamics, which can severely worsen intraglomerular pressure and lower GFR. NSAIDs like diclofenac, ACEIs like captopril, and ARBs like valsartan can have this effect Milanesi *et al.* (2019); Sudjarwo *et al.* (2019). Additionally, afferent arteriole vasoconstriction is a dose-dependent side effect of tacrolimus and cyclosporine. Cytotoxicity in the renal tubules is another mechanism of drug-induced nephrotoxicity. Proximal tubule cells are particularly vulnerable due to their active secretion and reabsorption processes and ability for biotransformation. Additionally, the proximal tubule epithelium consistently expresses a wide variety of functional transporters and metabolic enzymes that collaborate to facilitate renal drug clearance. Renal drug transporters are tightly packed, making proximal renal tubules more sensitive to hazardous substances such as antiretroviral medications and cisplatin (Qu *et al.,* 2018). Interstitial nephritis and glomerulonephritis are also mechanisms of drug-induced nephrotoxicity. Glomerulonephritis is an inflammation of the glomeruli resulting from a variety of nephrotoxic substances, while interstitial nephritis can be brought on by an anaphylactic reaction to a medicine. Analgesics, Chinese herbal medicine, and cyclosporine are among the medications that can lead to chronic interstitial nephritis. It is important to diagnose this problem as soon as possible because it could proceed to end-stage kidney disease (Suzuki *et al.,* 2009).

The topic of drug-induced nephrotoxicity has gained attention in recent years, particularly with regards to apoptosis and oxidative stress. Apoptosis is a complex process that can be triggered by both internal and external factors, and it involves intracellular enzymes such as caspases, AIF, and cytochrome c. The intrinsic pathway, involving the activation of proapoptotic Bcl-2 family proteins Bax and Bak, has been identified as the main pathway for apoptosis in cisplatin nephrotoxicity. The activation of Bax is connected to a shift in the ratio of pro- to anti-apoptotic Bcl-2 proteins and blocking the morphological change can reverse mitochondrial damage and stop cisplatin-induced apoptosis. Gentamicin-induced apoptosis is largely the result of caspase-dependent apoptotic signaling, and oxidative stress is a significant contributor to the nephrotoxicity of both cisplatin and gentamicin. Reactive oxygen species (ROS) are produced under these pathological circumstances, and ROS buildup can occur due to cisplatin's reaction with molecules containing thiols, mitochondrial malfunction, and the cytochrome P450 system. Similarly, hydrogen peroxide and superoxide anion production increase in response to gentamicin, and interventional drugs have been shown to lessen histological indications of damage (Amudha & Pari 2011; Strasser, O'Connor, & Dixit 2000; Lee *et al.,* 2001; Jiang *et al.,* 2006; Brooks *et al.,* 2007; Baliga *et al.,* 1997; Kruidering *et al.,* 1997; Liu & Baliga 2003; Walker *et al.,* 1999).

PEDALIUM MUREX LINN

Pedalium murex (*P. murex*) is a shrubby herbaceous plant belonging to the Pedaliaceae family found in India, tropical Africa, Sri Lanka, Pakistan, and Mexico. The plant has many branches with alternate, repandangulate leaves and axillary flowers with two yellow glands on the pedicel. Its taxonomical classification includes the Kingdom Plantae, Division Magnoliophyte, Class Magnoliopsida, Order Lamiales, Family Pedaliaceae, and Genus *Pedalium L*. The plant is known by different names in different regions based on its geographical location. Extensive phytochemical analyses have revealed the presence of numerous components, including flavonoids, triterpenoids, saponins, fatty acids, tannins, vitamins, proteins, steroids, sugars, vanillin, and ursolic acid. The plant has been shown to have several pharmacological activities, including antifungal, antibacterial, antioxidant, antidiabetic, and hepatoprotective effects. The seed oil of *P. murex* has been found to be a good source of protein and fat (Singh *et al.,* 2010; Thamizh Mozhi *et al.,* 2011; Sahayaraj *et al.,* 2008).

Phytochemical constituents of *P. murex*. Numerous phytochemical components, including flavonoids, triterpenoids, Saponins, fatty acids, tannins, vitamins, proteins, steroids, sugars, vanillin, and ursolic acid, were found in the plant after extensive phytochemical analyses. According to qualitative phytochemical screening, petroleum ether extract contains greater levels of steroids and sterols and moderate amounts of flavonoids, glycosides, phenols, alkaloids, carbohydrate s, gums, terpenes, proteins, and mucin (Subramanian & Nair 1972). So far, several substances have been extracted and described from several parts of P. *murex*. Two novel substances were also identified namely triacontanyldotriacontanoate, and 2', 4', 5'-trihydroxy-5, 7-dimethoxyflavone were present in the ethanolic extract of fruits. From chemical and spectral data, rubusic acid, luteolin, nonacosane, triacontanoic acid, tritriacontane, and sitosterol- beta-D-glucoside were also extracted and characterized. From the plant's leaves, fruit, and stem, researchers were able to isolate the Pedalitin (5, 6, 3, 4-tetrahydroxy-7-methoxyflavone) a flavonoid. In addition, it was observed that the fruit and stem of *P. murex* contained the dinatin (5, 7, 4-trihydroxy-6-methoxy flavones) (Zafar & Gupta 1989; Kapoor & Rahul 2006).

Other phytochemical components in *P. murex* comprise phenolic acids, lipids including vanillic acid, protocathechic acid, ferulic acid, and caffeic acid

as well as amino acids such histidine, glutamic acid, and aspartic acid. Other substances, including luteolin and 2, 4, 5-trihydroxy-5, 7-dimethoxyflavone from fruits, as well as hispidulin 7-Oglucuronide, Pedalitin 6-Oglucoside, hispidulin, diosmosing 7-O-glucuronide, and diosmosing, have also been found to be extracted from the plant's leaf section. Additionally, ascorbic acid levels in the plant were evaluated, and it was shown that fruits had the most ascorbic acid (Thamilmani *et al.*, 2007). It was estimated that the plant contained considerable amounts of total nitrogen, organic carbon, and total protein. A significant number of inorganic components, such as the Zinc and Potassium contents discovered in the leaves and the Barium content in the fruits, has also been observed for *P. murex* in addition to the organic chemicals (Rao, 1994). The plant's seed oil was also examined for its primary component, amino acid and fatty acid composition and was discovered to be a great source of both protein and fat. Low levels of unsaturated fatty acids were found in the fatty acid profiles of the fat from these oil seeds (Patel *et al.*, 2011) (Fig. 1).

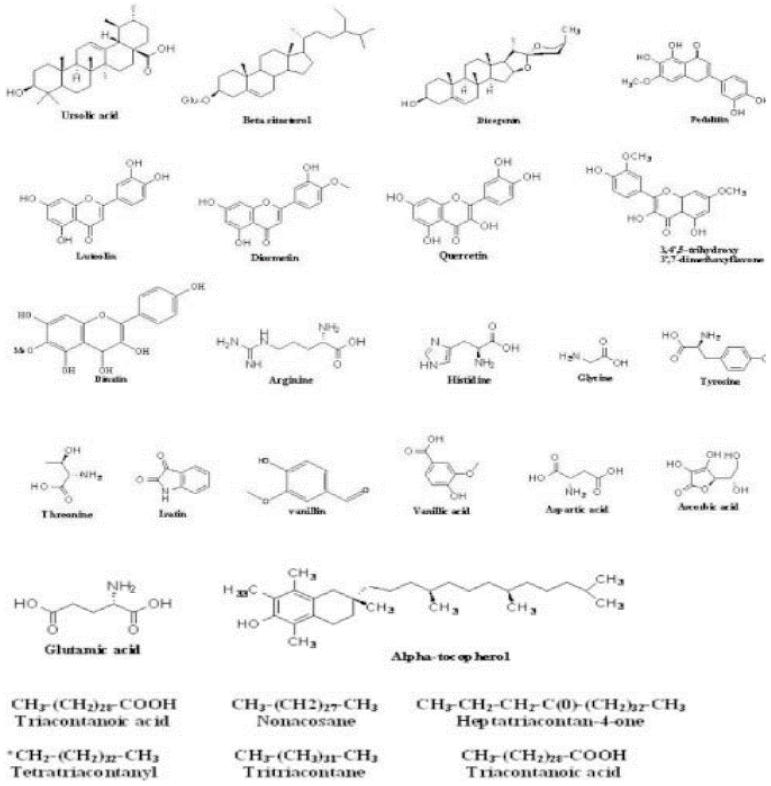

Fig. 1. Structures of the Phytoconstituents isolated in the *Pedalium murex.*

Pharmacological activities:

Acute Toxicity study. The *P. murex* plant was found to be safe up to a maximum dose of 2260 mg/kg, orally in mice according to research on its acute toxicity. According to CPCSEA criteria, the study was conducted on male Swiss albino mice weighing 20–25 g, which were given an oral dose of an ethanolic extract of *P. murex* and monitored for 48 hours for any signs of toxicity. According to Karber's procedure, the LD50 was determined to be 2260 mg/kg, oral dose. The dosages for additional pharmacological research were set at 250 mg/kg, p.o. based on these findings. Male Swiss albino mice were given alcohol-based *P. murex* extracts orally, however even after 48 hours of observation; there were no adverse effects that could be seen up to 2260 mg/kg, p.o. body weight (LD50 >2000 mg/kg) (Shelke *et al.*, 2009).

Nephroprotective potential. Wistar rats subjected to a Cisplatin-induced nephrotoxicity model were used to test the nephroprotective efficacy of the ethanolic extract of the dried *P. murex* fruits. Blood urea, Serum creatinine, and changes in body weight were used as markers of kidney damage. As a standard medication, cystone was taken. At an oral dose of 250 mg/kg, the results showed a substantial change in serum creatinine levels, body weight, and urea levels. It was also observed that the ethanolic extract of *P. murex* dried fruit showed considerable nephroprotective effect when compared to standard (Adikay *et al.*, 2010). The effectiveness of *P. murex* fruit extracts in preventing cadmium chloride-induced (3 mg/kg/s.c.) nephrotoxicity in rats was also assessed using serum creatinine, blood urea nitrogen, lipid peroxidation, urinary protein, urine to serum creatinine ratio, catalase, and gluthione in the kidney as the primary parameters. The outcome shows that aqueous and ethanolic extract with $CdCl_2$ substantially and dose-dependently reduced the kidney damage (Patel *et al.*, 2011).

Antioxidant Potential. Nitric oxide scavenging, reducing power, hydrogen peroxide scavenging, deoxyribose scavenging, and total antioxidant tests were used to test the antioxidant properties of various *P. murex* fractions in vitro. When compared to other fractions, the ethyl acetate fraction was shown to have strong reducing and

antioxidant power (Srinivas *et al.,* 2011). The antioxidant potential of methanolic extract of fruit of P. murex has also been revealed in vivo using carbon tetrachloride-induced hepatotoxic disease model in rats at an oral dose of 70 mg/kg, body weight for 12 weeks. It was discovered that antioxidant enzyme activity decreased in CCl4-induced rats and returned to near normal, indicating its antioxidant activity. These enzymes include Glutathione reductase, superoxide dismutase (SOD), Glutathione peroxide, and catalase (CAT) (Saha & Paul 2017).

Aphrodisiac Potential. The petroleum ether extract of *P. murex* was examined for its aphrodisiac potential, and it was discovered that it has the capability to enhance arousal and to treat ethanol-induced germ cell impairment and impotence in male rat models. In comparison to the ethanol-treated group, different doses of the *P. murex* extract (oral dose of 200 mg/kg and 400 mg/kg,) demonstrated a positive and substantial increase in mating, mounting behaviour, total body weight, sperm motility, percentage of pregnancy, and litter size. Additionally, it was noted that the levels of testosterone, total protein, and total cholesterol had all dramatically increased (Saha & Paul 2017). Several other miscellaneous activities were also reported for different kinds of extracts of various parts of *P. murex.*

HYGROPHILA AURICULATA (*K. SCHUM*) HEINE

Hygrophila auriculata (*K. schum*) Heine, a member of the Acanthaceae family, can be found in tropical and subtropical regions of India. Its root and seeds are used as a tonic for various ailments, including asthma, dysentery, tubercular fistula, and cancer. The plant's root, leaf, and seed have also been traditionally used to treat inflammatory conditions like jaundice, urinary infections, hepatic obstruction, oedema, gout, diabetes, and bacterial infections (Nadkarni & Nadkarn 1982). This subshrub grows in marshy areas along waterways and has eight leaves and six spines at each node. The leaves grow in whorls, with the outer pair being bigger, lanceolate, scaley, and small stalk with slightly dentate margins and sharp, straight, or curved spines. The plant produces axillary whorls of flowers, and the leafy bract and bracteoles are present. The four lobes on the calyx are not evenly spaced out. The centre lobe of the lower lip has a yellow palate, while the corolla is purple in colour. The flower has five gamopetalous petals and is unevenly 2-lipped. Four stamens, in two pairs, with varying filament lengths; diverging anthers; a two-celled ovary with four ovules in each cell. The fruit is a dehiscent capsule shape (Shanmugasundaram and Venkataraman 2006).

The plant's taxonomic classification is as follows:

- Kingdom - Plantae
- Division - Angiospermae
- Order - Lamiales
- Family - Acanthaceae
- Genus - Hygrophila
- Species - Auriculata

Hygrophila auriculata has several vernacular names depending on the geographical location, including Okilaksa in Sanskrit, Kuliyakhara in Bengali, Enugu palleru in Telugu, Ekharo in Gujrati, Talmakhana in Hindi, Kolavali in Kannada, Talikhana and Kasandra in Marathi, and Golmidi in Tamil (Bera *et al.,* 2017; Kshirsagar *et al.,* 2010; Gupta *et al.,* 2013).

Phytochemical constituents of *H. auriculata*. The exploratory phytochemical examination of the aqueous and other fractions of *Hygrophila auriculata* revealed that the main phytochemical constituents were terpenoid saponins, flavonoids, and tannins. Chemical analysis of the n-butanol fraction showed tepenoids to be present. It has been found that the plant *Hygrophila auriculata* is exceptional in terms of the amount of terpenoids and flavonoids that it contains (Choudhary & Bandyopdhyay 1980). The proteins that are present in the seed of *Hygrophila auriculata* was found to contain all the required amino acids and were analogous to those of groundnut protein, according to Thanki and Thaker's study on the amino acid content of the seeds (Talukdar *et al.,* 2023).

According to study the methanolic extract of *H. auriculata* was found to have strong antioxidant and anti-diabetic properties. This investigation offers empirical support for the hypoglycaemic and antioxidant effects of *H. auriculata.* This plant may undoubtedly be utilised to create medications that target oxidative stress-related conditions like diabetes. Clinical research to assess the extract's safety and clarify its mechanism of action is required before it is possible for humans to use the extract (Hussain *et al.,* 2019). According to the literature, there are several phytoconstituents present in the seeds, including betasitosterol, botulin, lupeol, apigenin 7-O-glucoside asteracanthine, apigenin 7-O-glucuronide, and asteracanthicine. Four known aliphatic ester compounds that may be significant from a chemotaxonomic perspective were reported together with the isolation and characterisation of a new phytoconstituents.

Pharmacological activities:

Toxicity studies. An intraperitoneal injection of *H. auriculata* petroleum ether extract at doses of 40 and 80 mg/kg body weight has been shown to impact mice's metabolism, haematological parameters, metabolism, and kidney and liver functions (Mazumdar *et al.,* 1996). However, daily doses up to 4 mg/kg and weekly doses up to 20 mg/kg fail to cause any toxicity symptoms or warning indications. Furthermore, in another investigation, rats given fixed dosages of up to 2000 mg/kg between methanolic extracts of leaves of *H. auriculata* for fourteen days showed no signs of toxicity (Neharkar & Pandhare 2015). Clinical studies on 48 patients in a multicenter, double-blind homoeopathic pathogenetic trial revealed that it was a safe therapeutic option for treating gastroenteritis, urticaria, stomatitis, nausea, conjunctivitis, frontal sinusitis, and intermittent fever (Rakshit *et al.,* 2014).

Hepatoprotective Potential. Histopathological analysis and kidney function tests revealed that the gentamicin-induced nephrotoxicity in male Sprague-Dawley rats' proximal tubular cell death was therapeutically retrieved after daily doses of 250 mg/kg ethanol extract of leaves of *H. spinose* (Singh & Handa 1995). whereas in another study, methanol extract of *H. spinosa* considerably lowered blood urea and serum creatinine levels and corrected adverse

histopathological changes, this effect could be a result of secondary metabolites in the *H. spinosa* extract having antioxidant activity, which would increase kidney enzyme performance (Ingale *et al.*, 2013).

Antioxidant Potential. *H. auriculata* seeds are traditionally utilized to treat inflammatory ailments. Sunilkumar and Klausmuller (1999) checked 28 various species of Nepalese traditional medicines for an inhibitory effect on lipid peroxidation. They found that the plant inhibited lipid peroxidation with an IC50 Value of 20 g/ml (KC & Müller 1999).

Diuretic Potential. Using the techniques outlined by Lipschitz *et al.* (1943) the diuretic ability of the alcoholic, aqueous and various fractions of the alcoholic extract of the entire plant of *Hygrophila auriculata* (*K. schum*) Heine was assessed (1943). Various groups of Wistar albino rats were given single (200 mg/kg) oral doses of alcoholic extracts or fractions to test the diuretic impact. In the trial, furosemide (10 mg/kg) was employed as a positive control. The n-butanol fraction (200 mg/kg) significantly raised the urine production among the other fractions. The pattern of diuresis brought on by the n-butanol fraction resembled that brought on by furosemide almost exactly (Hussain *et al.*, 2009).

CNS Activity. The petroleum ether extract of the root of Hygrophila spinosa was subjected to a chemical investigation by Mazumdar *et al.* (1999), which revealed the existence of active ingredients such lupenone and lupeol. Additionally, they noted that administering crude petroleum ether extract intravenously (intraperitoneally) to mice enhanced the sedative-hypnotic effects of chlorpromazine, phenobarbitone, diazepam, and chlordiazepoxide and prevented strychnine-induced convulsions (Mazumder *et al.*, 1999).

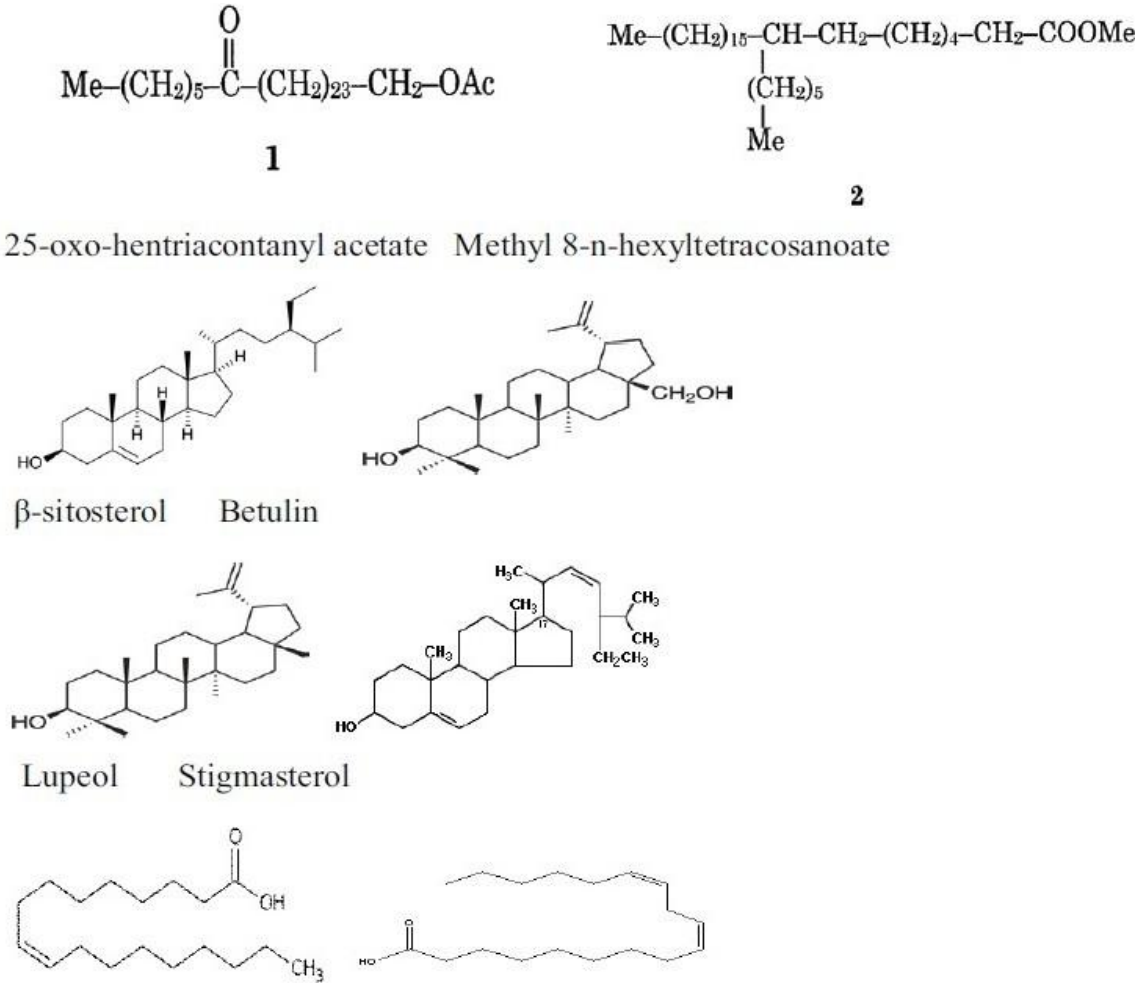

Fig. 2. Major phytochemical constituents of *H. spinosa*.

CONCLUSIONS

After reviewing the available literature, it can be concluded that *Padalliu murex* Linn and *Hygrophilla auriculata* may have potential for treating drug-induced nephrotoxicity. The phytochemical constituents of both plants have been shown to possess hepatoprotective and antioxidant properties, which could be beneficial for kidney function. Additionally, the diuretic potential of *Hygrophilla Auriculata* suggests that it may help to eliminate toxins from the body. However, it should be noted that further research is needed to establish the safety and efficacy of these plants in treating nephrotoxicity.

FUTURE SCOPE

The future scope for this review on herbal remedies for drug-induced nephrotoxicity is vast and holds several promising avenues for further investigation. Mechanistic studies at the cellular and molecular levels should be conducted to unravel the underlying

pathways through which these herbal remedies exert their nephroprotective effects, potentially leading to the identification of novel drug targets.

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Conflict of Interest. None.

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