Conventional medicines used for kidney protection in Bangladesh: a review

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Abstract

To describe the kidney's response to specific substances, such as dangerous compounds and pharmaceuticals, the term "nephrotoxicity" is employed. When the body is subjected to toxins or medications, nephrotoxicity is among the most prevalent side effects. Numerous medical treatments, including anti-cancer medicines, antibiotics, and some Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), can cause nephrotoxicity. This review discusses a variety of drugs that can preserve the kidneys. The nephroprotective qualities of natural substances, medicinal plants, and dietary components have been examined. Medicinal plant chemicals have a significant role in pharmaceutical research. A wide range of herbs has been shown to have nephroprotective effects. Treatment of renal calculi, prevention of diabetic nephropathy, and reduction in tubular damage were all achieved. Plant-based therapies contain phytochemicals that have nephroprotective properties. Plants with nephroprotective activities have been reported on cisplatin, gentamicin, adriamycin, and urolithiasis, caffeic acid phenethyl ester assists in nephrotoxicity and free radicals radical scavenging activity, which may be utilized to prevent and treat kidney damage. In the end, investigating traditional medicines from Bangladesh that contain kidney-protecting plants is an intriguing new avenue of inquiry that could lead to effective new therapies for renal illnesses. Maintaining kidney health and enhancing the lives of countless people is only possible with further investigation into the beneficial effects of plants on renal function. However, it is crucial to find a middle ground between ancient practices and evidence-based modern medicine, stressing the importance of making educated decisions and following expert guidance to guarantee uncompromised kidney health.

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Key words: nephroprotective, kidney diseases, cisplatin, nephrotoxicity, gentamicin.

Contributions: SAZ, came up with the initial concept for the review paper, conducted the initial literature search, and drafted the manuscript; MIU, drew the compound structure; SSI and JN, reviewed and edited the manuscript for scientific accuracy and rigor, made the necessary corrections in the write-up and gave the final approval for the submission of a revised version. All authors have read and approved the final manuscript, and agreed to be held accountable for all aspects of the work.

Conflict of interest: the authors declare no potential conflict of interest.

Funding: none.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.

Received: 17 April 2023.
Accepted: 28 July 2023.
Early access 12 Septmber 2023.

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Licensee PAGEPress, Italy
Infectious Diseases and Herbal Medicine 2023; 4:328
doi:10.4081/idhm.2023.328

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Introduction

Numerous medicinal plants used in traditional medicine in Bangladesh could result in nephrotoxicity. This paper discusses the nephrotoxic qualities of various plants, their active ingredients, mechanisms of toxicity, hazards, and strategies for prevention. For traditional healthcare systems to employ medicinal plants securely, these factors must be understood. Bangladeshi groups use traditional medicine widely. Research has demonstrated that several therapeutic herbs damage the kidneys. Chemicals can damage the kidneys and impair renal function, generating nephrotoxicity. Bangladesh's nephrotoxic medicinal plants possess active constituents; the nephrotoxic effects of these medicinal plants have been attributed to specific bioactive compounds present within them. For example, aristolochic acids, alkaloids such as aconitine, have been linked to renal toxicity. The nephrotoxic effects of these medicinal plants may be attributed to various mechanisms, including oxidative stress, inflammation, and direct cellular toxicity. For instance, aristolochic acids found in *Aristolochia spp*. can lead to DNA adduct formation and renal tubular damage, resulting in nephrotoxicity.[1] Due to dose and exposure length, nephrotoxicity may differ across individuals: nephrotoxic medicinal herbs may cause kidney damage at larger doses and longer durations. Individuals with pre-existing kidney disorders may be more susceptible to nephrotoxic effects. The use of certain medicinal plants can reduce nephrotoxic threats. However, natural objects should be supervised to ensure their safety and effectiveness. Healthcare providers and the general public must be educated about the potential nephrotoxic effects of

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specific medicinal plants. Recent worldwide kidney illness data indicate an alarming pattern, highlighting the need for extensive research and effective therapies. Based on present motifs, the burden of renal disease is likely to increase in the future. This expected increase is due to population growth, aging, and the increased incidence of risk factors like diabetes, hypertension, and obesity. These predictions show that kidney disease burden reduction must be prioritized. Plants include a diverse spectrum of bioactive metabolites that serve as antioxidants, anti-inflammatory agents, diuretics, anticancer properties, and antibacterial agents.[2-3] Moreover, plant-derived nephroprotective medicines alleviate conditions such as nephrotic syndrome, altered intraglomerular neovascularization, tubular apoptosis, and renal insufficiency.[4] Earlier studies have examined the application of plants and phytonutrients as nephroprotective agents, offering a vital understanding of how naturally occurring substances or single molecules interact with molecular pathways to prevent kidney damage.[5] Plants and their derivatives have been exploited as healthy alternatives for functional foods, herbal medications, natural remedies, phytomedicine, and nutraceuticals for the last two decades.[6] A plant-based diet enhances renal pathophysiology in mild proteinuria and nephrotic syndrome patients. The kidney eliminates metabolic waste such as carbohydrates, proteins, and fat. This makes it the most important organ for human health. Most processes depend on tubular cells. Converting glucose into glucose is called gluconeogenesis. People often encounter dangers when taking walks. Pathophysiological conditions include increased metabolic activity, tubular elimination of fluid concentrations, and renal tubule blood flow. Organs make the body more toxic. Due to medicines and other chemicals' cytotoxic impact, kidney function quickly declines. In nephrotoxicity, the kidneys are still unable to perform their regular positions. Adverse import effects on renal function are known as "nephrotoxic".[7] Substances can damage the kidneys through nephrotoxicity. The kidneys regulate fluid and electrolyte balance and filter waste. Nephrotoxic substances can damage kidney tissue, impairing kidney function (*Supplementary Table 1*).[8-11]

Crystal necrosis, glomerular damage, renal tubule toxicity, and inflammation can cause nephrotoxicity. Molds and fungi, antibiotics, cancer drugs, lead, arsenic, mercury, and other substances can induce nephrotoxicity. Necrosis and renal failure can be caused by internal and environmental factors. Polycystic Kidney Disease (PKD), Tubular Cell Death (TCD), and kidney stones are other kidney disease risk factors. But various inherent variables may lead to renal problems like glomerulonephritis, polycystic kidney disease, sepsis, pulmonary failure, and liver failure. Malignancy-related kidney disease is diagnosed and characterized by renal pathology.[12] The renal pathology and nephrotoxicity are distinct when the kidney is not afflicted by drug-induced damage. Nephrotoxicity is comparable to kidney problems in numerous manners. Both can be attributed to the structural and functional changes in the nephrons that result from injury to or death of renal cells. Those are present-day conditions. Kidney cells are affected by glomeruli, interstitial tubules, and renal arteries. There are millions of nephrons in a functioning kidney. Its fundamental function is to remove waste from the body, maintain fluid balance, and regulate blood pH and hormones that encourage red blood cell formation. In particular, it influences bone health and the immunological system.[13] When it comes to dosing, contraindications, and side effects, nephrotoxicity studies on plants in Bangladesh have produced conflicting results. Certain plants may be nephrotoxic if taken in large enough quantities, according to the findings of some research. Many of these studies warn against excessive or irresponsible usage of these plants, whether for medical or culinary purposes.

Materials and Methods

Comprehensive searches are conducted in electronic databases such as PubMed, Scopus, Web of Science, and Google Scholar. Additionally, specialized databases related to ethnobotany and traditional medicine in Bangladesh. The search strategy was used for relevant keywords and combinations related to nephrotoxic plants, nephrotoxicity, renal toxicity, and Bangladesh. Databases were searched for articles published between 2000 and 2020 for this research. We classify nephrotoxic plants, chemical substances that cause toxicity, experimental methods, and study results. Structured data will be synthesized. Narratives, tables, and charts may be used to summarize and detect patterns in Bangladesh's nephrotoxic plants (Figure 1).

Inclusion criteria

To be included in the review article, studies must meet the following criteria: i) study types, both primary research studies (observational, experimental, and clinical studies), and review articles that discuss nephrotoxic plants found in Bangladesh will be considered; ii) plant source, studies reporting on plants found in Bangladesh that are known or suspected to have nephrotoxic properties will be included; iii) nephrotoxicity, studies reporting cases or evidence of nephrotoxicity associated with the use of these plants in humans or animals will be considered.

Exclusion criteria

Studies failing to meet the following criteria will be excluded from the review: i) plants from other regions, studies focusing on nephrotoxic plants from countries other than Bangladesh will not be included; ii) non-peer-reviewed literature, grey literature, conference abstracts, and unpublished reports will be excluded; iii) irrelevant studies, studies that do not specifically investigate nephrotoxicity or do not pertain to plants found in Bangladesh will not be considered; iv) non-human studies, articles reporting solely on *in vitro* or animal studies without any relevance to human nephrotoxicity will be excluded; v) inaccessible full-text, studies with no available full-text despite extensive efforts to access them will be excluded. This review article intends to provide an extensive and trustworthy overview of the nephrotoxic plants in Bangladesh, the risks they bring about, and the areas that need more study to safeguard the public's health and safety.

Discussion

Nephrotoxic agents

Toxic drugs, industrial chemicals, and environmental contaminants can cause kidney disease or kidney malfunction in the human body. The kidney is susceptible to the impacts of pollutants on the environment since it has an excretory role. Potassium and magnesium are two electrolytes that inhibit water from being absorbed by the kidneys, causing severe damage and increasing blood electrolyte levels. To avoid long-term exposure to exogenous and endogenous dangerous compounds, such as unlawful abortifacients and cancer-fighting medications, it is necessary to eliminate all extra urine and waste from the patient's body. The manifestation of the illness can be traced back to any one of these agents. Nephrotoxic compounds include metals, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), solvents, glycols, cancer therapies, aminoglycosides, and antibiotics, to name a few. The kidney's proximal tubular cells perish when metals like mercury

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and fumes enter the body. Necrosis and failure of renal cells are triggered by bismuth. They're the metals that destroy kidney cells: thulium, barium, and potassium. Inhibiting the release of potassium from cells results in hypokalemia, which can be life-threatening. Several NSAIDs induce kidney damage, including interstitial nephritis and acute renal failure. They potentially cause potassium buildup and hypertension.[14]

The most common organic solvents are oxalate of calcium, toluene, CCl_4, and tetrachloroethylene. When CCl_4 is transformed, two new free radicals are formed: trichloromethyl and trichloromethyl peroxyl. Free radicals have always been detrimental to cells, and renal cells are particularly vulnerable to free radicals. Hypertension results from renal tubular necrosis and renal tubular injury. The tubular necrosis generated by tetrachloroethylene intoxication results in renal failure.

Glycolic and oxalic acids are synthesized from ethylene glycol, and the crystals formed are then deposited in the renal tubules as wastage.[15]

This stumbling block progresses to renal failure in the long run. Interstitial inflammation can lead to death unless crystals are formed. It is possible to simultaneously suffer from hemorrhagic, proteinuric, or oliguric urine incontinence. Antimetabolites, alkylating agents, and radiocontrast agents are only a few anti-cancer drugs available.[16]

Additionally, cancer-fighting antibiotics are available. According to Cisplatin's ability to cause severe nephrotoxicity, its use is restricted (Figure 2).[13,17]

This medication has substantial clinical restrictions due to its nephrotoxicity. Generates reactive oxygen species when ingested. Renal failure develops as a direct consequence. Examples of antibacterial agents include acyclovir, sulfadiazine, and rifampicin. The three phases of drug-induced nephrotoxicity may be summarized as follows: the initial phase, in which the kidneys are exposed to dangerous materials; the second phase, in which the kidneys are protected; and the third phase, in which the kidneys are damaged. They become inactive due to the presence of substances, including lipids, proteins, DNA, and RNA. This inactivation occurs in Reactive Oxygen Species (ROS) and free radicals, which have a damaging impact on the kidney. There is a lot of pressure on the semipermeable barrier. During the propagation stage, toxicants hinder the process from continuing. A wide variety of factors can cause renal injury.[18]

Many drugs, for example, can induce kidney damage in a multitude of ways, including direct cell toxicity and high drug doses. Certain medications, such as aminoglycosides and amphotericin B, might have serious adverse effects if used in excess. As a result of lysosomal dysfunction and cell enlargement associated with drug saturation in the renal tubules, certain medications become toxic. Aside from medication-related nephrotoxicity, patient-specific variables can also raise the risk. Males and females have varied body mass, and females with less total body water have the highest nephrotoxicity risk because of this abundance variation. Inflammatory damage can be produced by genetic alterations in the human immune system, which raises the risk of renal toxicity. Patients with liver disease, heart disease, or other metabolic diseases are at greater risk of nephrotoxicity. As blood and cellular activity rise, the kidney becomes the decisive risk factor for nephrotoxicity, along with its increased vulnerability.[19]

Nephroprotective drugs

Traditional medicines have a significant role in providing essential healthcare. The World Health Organization (WHO) estimates that over 80% of the world's population consumes conventional drugs and that these treatments offer substantial health advantages, particularly in developing countries. Chemicals from these origins can generate a massive spectrum of medications. A broad spectrum of ailments can be prevented using traditional functional drugs. Several studies have found bioactive components in these plants to be beneficial. There are medicinal compounds in these plants that can help people stay healthy and avoid illness. Many kidney illnesses can be effectively treated using nephroprotective medications from plant sources. There has been a rise in the

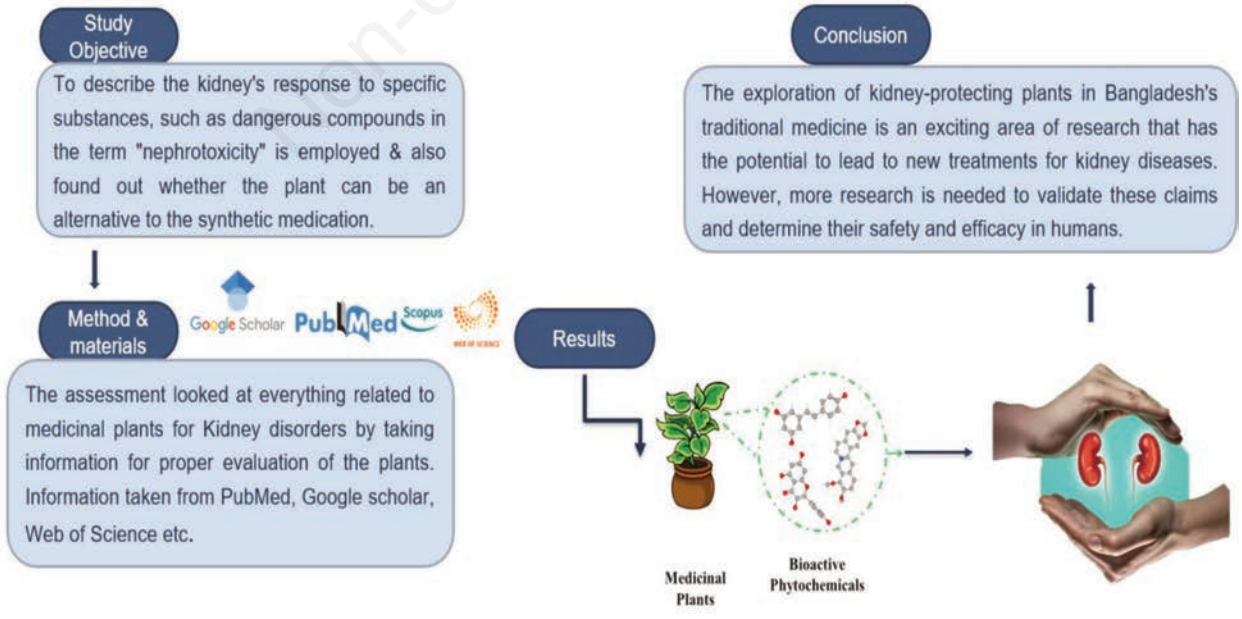

Figure 1. Flowchart of research methodology.

need for safer and less affordable plant-based therapeutics as a reaction to the problem of drug resistance and side effects. The growing popularity of herbal treatments has resulted in patients being compelled to utilize both pharmaceuticals and homeopathic therapies. The merging between prescription medications and natural remedies might have adverse outcomes.[20]

Alkaloids, glycosides, carotenoids, and other phenolic compounds are found in a wide range of medicinal plants. All of these substances have antioxidant capabilities. Many kidney issues can be addressed using the therapeutic characteristics of these plants because of their ability to combat oxidative stress. Search engines based on traditional knowledge will be vital. But it will also make it a lot simpler to undertake research on natural products to reinvent the drug development process more precisely and securely (*Supplementary Table 2*).[21-37]

Use of phytoconstituents derived from several medicinal plants as nephroprotective medications

Artemisia annua

Treatment of protozoal infection using the green herb *Artemisia annua (Asteraceae)* has been documented. Essentially, it is an antimalarial medication.

Fever and hemorrhoids were two of their traditional uses. Intrarenal, rectal, and oral formulations are now available for *Plasmodium falciparum* malaria treatment. In the presence of terpenoids, the plant alcohol extract has been demonstrated to be nephroprotective. Terpenoids like artemisia ketone-pinene are plentiful in the plant. In addition to being called sweet wormwood, the crude drug's extract is an excellent source of the naturally occurring sesquiterpene artemisinin. In the fragrance business, sweet wormwood is used as a source of essential oil and is an excellent product to use as such.

There is a more significant concentration of flavonoids in the leaves of these plants, which have antiviral and anti-oxidant characteristics.[38]

Curcuma xanthorrhiza

It is found on the Indonesian island of Java, in Malaysia, Thailand, and China. It's recognized as Java Ginger. It includes the sesquiterpene xanthorrhizol identified in *Curcuma xanthorrhiza*, which has antibacterial, anti-cancer, and anti-inflammatory properties. The plant's stem is employed to treat postpartum vaginal bleeding caused by inflammation. In 2005, Kim *et al*. determined that it would have nephroprotective characteristics after doing an investigation.[39]

Zingiber officinale

Many countries have long utilized ginger as a medicinal herb, making it the most common term for this plant. Its principal source is *Zingiber officinale (Zingiberaceae*), which gently imparts ginger's distinctive flavor. It is made up of the same phenols. According to reports, anti-emetic, carminative, anti-inflammatory, and peripheral circulation stimulants. Both aqueous and ethanolic

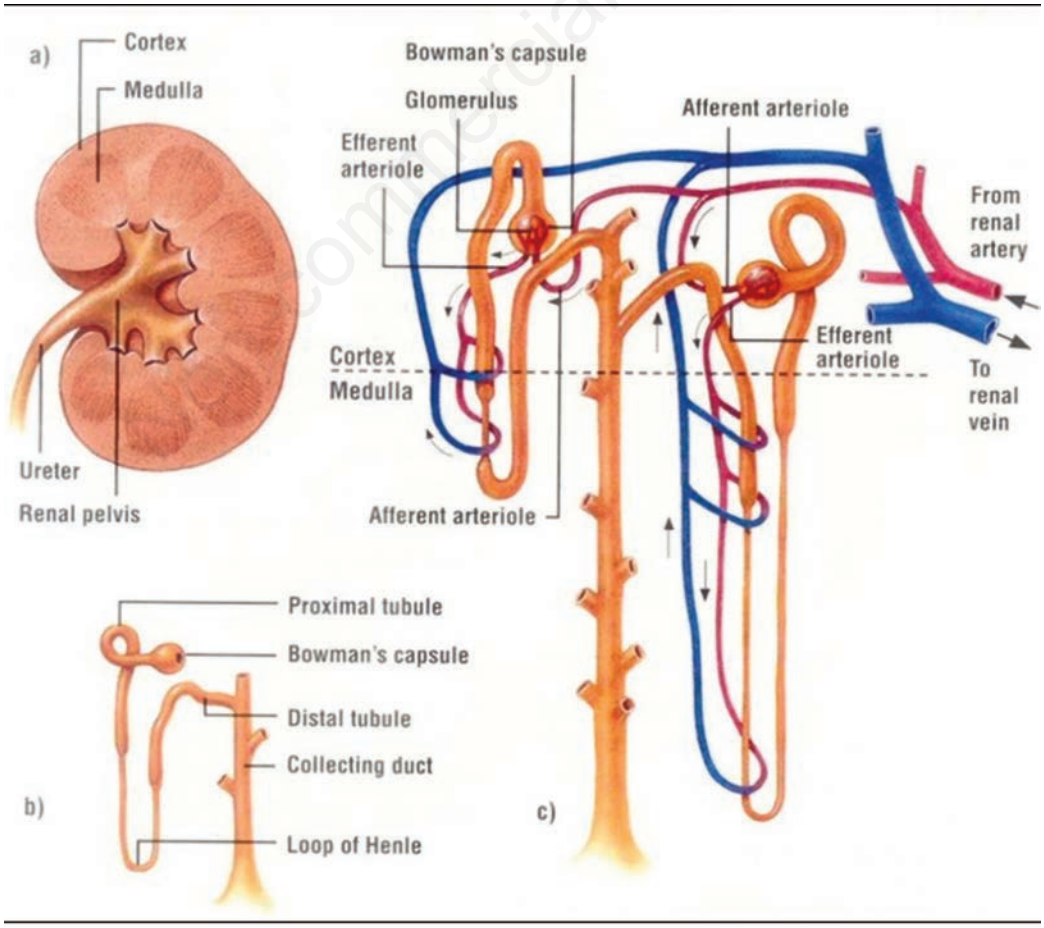

Figure 2. Structure of the kidney.

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ginger extracts are beneficial against cancer and in the treatment of doxorubicin-induced kidney damage.[40]

Aervalanata

A typical weed in tropical India is *Aervalanata (Amaranthaceae),* which is abundant throughout the region. This species has different populations in Africa, Sri Lanka, and the Philippine Islands. It is utilized as an expectorant, anthelmintic, and diuretic in medicine. To cure diarrhea and kidney stones, the leaves of this plant are traditionally utilized. To cure snakebites, this plant's root is employed. In particular, it is used to treat bleeding during pregnancy, a variety of skin illnesses, migraines, and the removal of kidney and gallbladder stones. It is used to keep the uterus free of bacteria. Toxic effects on the kidney are thought to be caused by flavonoid glycosides in this plant, such as 3-rhamnose and 3-rhamnogalactoside kaempferol, which may also be linked to nephrotoxicity-induced kidney damage. Nephrotoxicity triggered by cisplatin or antibiotics is typically performed with this drug.[41]

Curcuma longa

A member of the *Zingiberaceae* family of plants, including ginger, is *Curcuma longa*. The most common term for it is turmeric. For example, it is most commonly observed in India, China, and other regions with tropical weather. Many disorders can be treated using curcumin, the plant's primary chemical component. It is used as an antibacterial agent across several applications. Dried *Curcuma longa* is a common spice in Indian cuisine. There are two curcuminoids: Desmethoxycurcumin (DMC) and Curcumin (C). Bisdesmethoxycurcumin. These are the polyphenols that give turmeric its color. Everything from spices via dyes to flavorings to colorants includes it. Jaundice, bleeding, and colic in children can all be treated with this supplement. An antioxidant is also an anti-inflammatory.[42]

Andrographis paniculata

An *Acanthaceae* plant called as "King of Bitters" is *Andrographis paniculata*. Almost all of it is harvested in South Asia. The plant's leaves and roots heal a wide range of ailments. Both the diterpenoid andrographolide and the stigmasterol sterol are vital. In addition to treating cancer, heart disease, and diarrhea, this drug is also prescribed for a variety of other ailments. Inflammatory responses are reduced, and the liver is protected. *Andrographis paniculata's* chloroform extract is beneficial against nephrotoxicity because it possesses the active ingredients andrographolide and diterpenoids.[43]

Berberis vulgaris

Berberidaceae is a family that includes *Berberis vulgaris*. In southern Europe and western Asia, it is most often found. It was used extensively as a medicinal plant to cure a wide range of diseases in ancient times. Berbamin and iso-kaolin alkaloids are indeed found in the root of the plant and constitute an essential part of herbal medicine. Phosphoric acid and phenolic compounds are the building blocks of this chemical. Glycoside enzymes and anthocyanin, an antioxidant pigment, are also found in this food. Other beneficial properties include those for fighting cancer and preventing psoriasis. It may be used to cure jaundice, diarrhea, as well as malaria. Alkaloids in Berberis vulgaris exhibit nephroprotective properties.[44]

Camellia sinensis

The *Theaceae* family includes the *Camellia sinensis*. The plant is black, green, and oolong, among the most popular tea varieties. This drug was initially developed in China, although it is also accessible in India and Southeast Asia. Around the world, it is cultivated in tropical areas to supply this fruit and vegetable. It is the chemical components that make up catechins and flavonols. Four catechins are found in green tea: epicatechin, epigallocatechin, and epigallocatechin-3-gallate. Probiotics and antibiotics derived from this plant are all being used in the fight against cancer. Anti-nephrotoxic properties of catechin have been demonstrated.[45]

Ceratonia siliqua

The Leguminosae family member *Ceratonia siliqua* is endemic to Mediterranean climates and flourishes in hot, humid coastal conditions. The primary chemical components of carobs are polyphenols and tannins from the fruit. Anti-diarrheal characteristics of tannins extracted from the pulp in the cosmetics industry, the carob bean offers a wide range of applications. The phytochemical carob polyphenols have a critical role in kidney protection from nephrotoxicity.[46]

Nigella sativa

Nigella sativa may be found in the Middle East and Europe as a component of the Ranunculaceae family. These plants' seeds and oil are precious and used to cure a wide range of ailments. Carminative, diuretic, and antispasmodic properties are attributed to these seeds' bitterness. In particular, it can be used as an anti-odorant as well as a laxative. Analgesic qualities can be detected in the oil; t-anethol, sesquiterpene, and thymoquinone are active chemical components in this plant. Phytoconstituent thymoquinone, found in *Nigella sativa*, is crucial for the plant's health in repairing kidney damage induced by gentamicin.[47]

Panax ginseng

The *Araliaceae* family includes *Panax ginseng*. From China to Japan and Russia, the illness has spread. Asia is the region where it is most often cultivated. This plant is used as a medicinal herb in Japan, China, and Korea. It's a perennial with five-fingered leaves, and it has five fingers. Triterpenes, glycosides, and ginsenosides are the primary chemical components. Human health benefits include regulating blood sugar, reducing fatigue, and boosting the immune system.

In the context of cisplatin, ginsenoside Rh3, and Rh4 exhibit nephroprotective effects.[48]

Cicadae Cordyceps

A member of the *Clavicipitacea* family, *Cordyceps cicadae* is an ascomycete fungal species. High heights make the harvesting of this species complex. To compensate for the challenges, this medication has a high retail price. It was historically used to treat various ailments, including kidney illness, heart disease, and male and female sexual health difficulties. The plant's primary chemical constituents are polysaccharides, ergosterols, glycoproteins, cordycepin derivatives, and alfa aminobutyric acid. Only a few of its pharmacological qualities include antiarrhythmic, antimicrobial, insecticidal, anti-aging, neuroprotective, and Reno protective effects. Nephroprotective impacts are associated with the primary sterol (ergosterol).[49]

Literature review

Ashwagandha (*Withania somnifera* root) was tested to determine if it might protect Wistar albino rats from gentamicin-induced kidney damage.[12] The Department of Physiology at Sir Salimullah Medical College (SSMC) in Dhaka conducted an experimental study from July 1, 2010, to June 30, 2011. In this investigation, 35 Wistar albino rats ranging in age from 90 to 120 days and ranging between 150 and 200 grams were used. After 14

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days of acclimatization, they were divided into two groups: control (Group A) and trial (Group B) (Group B). Group A1 (baseline control) and Group A2 (additional control) comprised the control group, which was further broken into two subgroups (gentamicin-treated control group, consisting of 10 rats). The experimental group consisted of 15 rats (Group B- Ashwagandha pretreatment and gentamicin-treated group). The principal diet was supplied to all animals for 22 days. The antibiotic gentamicin (100 mg/kg body weight/day) was administered subcutaneously to group A2 during the last eight days (15th to 22nd). Group B was administered ashwagandha root extract (500 mg/kg body weight per day; orally) for 22 days and gentamicin subcutaneously (100 mg/kg body weight per day) during the final eight days of the experiment (15th to 22nd). All the animals were sacrificed on the 23rd day. Samples of blood and kidney were then collected. Serum urea and creatinine levels were determined using standard laboratory kits. One-way ANOVA and the Bonferroni test were used where appropriate for statistical analysis. To guard against gentamicin-induced nephrotoxicity, ashwagandha root (*Withania somnifera*) may be beneficial the mean serum urea, and creatinine levels were significantly ($p<0.001$) higher in gentamicin treated control group in comparison to those of baseline control. Again, these levels were significantly ($p<0.01$) lower in the ashwagandha pretreated and gentamicin-treated group (experimental group) when compared to those of the gentamicin-treated group (control). Ashwagandha (Withania somnifera) root may have some nephroprotective effect against gentamicin-induced nephrotoxicity.[8]

During the period between January 1 and December 30, 2018, the Physiology Department of Sir Salimullah Medical College (SSMC) in Dhaka carried out an experimental study. In this experiment, male Long Evans rats were subjected to gentamicin-induced nephrotoxicity, and aloe vera was given to some of the rats to test if it could protect the rats from this side effect. In this experiment, there were two groups: the control group, which was designated as Group A, and the experimental group, which was designated as Group B. Each group consisted of 45 healthy male long Evans rats that were between 90 and 120 days old and weighed between 150 and 200 grams (group B - the group that was pretreated with aloe vera and then given gentamicin). Control group A1 (also known as the baseline control group) served as the starting point from which control group A1 (also known as the gentamicin-treated control group) and the control group A2 were derived. In each of the groups, there was a mixture of 15 rats from the other group. On the first day of the experiment, the researchers determined the rats' starting weights by measuring their bodies. During thirty (30) days, every rat was fed the same diet. For the first thirty days of the experiment (day one through day thirty), group A1 was given nothing but a basic diet. In addition to consuming the regular diet from the 26th through the 30th day of the trial, participants in group A2 were given an intraperitoneal injection of gentamicin at a dose of 80 mg/kg each day (26th to 30th). Oral administration of Aloe vera at a dose of 200 milligrams per kilogram per day was given to the test subjects throughout the first 30 days of the study. After that, the test subjects received intraperitoneal injections of gentamicin at a dose of 80 milligrams per day for the final five days of the experiment (the 26th through the 30th). After the total mass of all the rats was calculated on day 31, they were all executed. The heart was punctured to get a sample of blood. To evaluate renal function, blood creatinine, and urea levels were analyzed. The post-hoc-Bonferroni test for statistical analysis followed the one-way ANOVA test. In this study, researchers have found that Aloe vera protects the kidneys against gentamicin-induced nephrotoxicity.[50]

Extracts of *D. alata* and *Morinagaolifera* showed promising and substantial effects in damaged kidneys of mice. Studies indicate that *D. alata* and *Moriegaolifera* extract may also be used to treat or prevent renal toxicity induced by cisplatin and other medications, with no negative impacts; consequently, it might be employed as a new combination treatment with cisplatin and other drugs to lessen renal damage. Cisplatin-induced kidney damage is prevented physiologically by RVE. Since these substances can be employed in people, it is imperative to discover which chemicals are capable of lowering cisplatin-induced renal damage. In rats, curcumin's nephroprotective impact was investigated. Nephrotoxicity triggered by Adriamycin (ADR) was examined in this study.[47]

Researchers have found that curcumin supplementation protects against ADR-induced kidney injury. According to the latest study, curcumin also protects against oxidative stress, enhances glutathione levels, and stimulates activity. Finding Curcumin as the best remedy for nephrotoxicity.[51]

The efficacy of the roots of *Andrographis paniculata* in treating renal disease was studied. The anti-hyperglycemic efficacy of a chloroform extract of these roots was examined in alloxan-induced diabetic rats. A remarkable anti-diabetic impact was shown in the research on chloroform extract. It was also discovered that this extract helped treat diabetic nephropathy. Research on human urolithiasis began with animal models, first in rats. Specifically, they investigated the role of Berberis vulgaris root bark's role in treating renal calculi, which is frequently utilized in homeopathy. The standardization of stone-forming components was made possible by the widespread use of Berberis vulgaris. Similarly, the serum creatinine levels were brought back into the normal range. It has been shown that Berberis vulgaris effectively influenced renal calculi.

Researchers studied the effects of ginsenoside on cisplatin-induced nephrotoxicity on cultured renal tubular cells. Cell viability was enhanced by the ginsenosides Rh4 and Rh3, which were seen to be dose-dependent. However, the cytoprotection mechanism is still unclear, and further research is needed to determine it (*Supplementary Table 3*).[52-60]

The use of time-tested, locally sourced remedies has a long history in Bangladesh. Among the many conditions that these traditional remedies have been used to treat for generations is kidney illness. Most people in Bangladesh can afford to get treatment with traditional medicine, hence it plays an important part in the country's healthcare system.

In Bangladesh, herbal treatments that use medicinal plants and their extracts are commonly used. The majority of the time, these medicines are taken orally in the form of decoctions, infusions, or powders, but on rare occasions, poultices or ointments may be used externally. Local healers and traditional medicine practitioners have kept alive the information and practice pertaining to these traditional remedies. For kidney diseases, traditional medicines in Bangladesh often include specific plants and herbal formulations known for their potential to alleviate symptoms and improve kidney function. These remedies are believed to work by promoting diuresis (increased urine production), reducing inflammation, and supporting overall kidney health. Some commonly used herbs for kidney ailments in Bangladesh include *Punarnava (Boerhavia diffusa), Gokshura (Tribulus terrestris), Varuna (Crataeva nurvala),* and *Shatavari (Asparagus racemosus).* One of the advantages of traditional medicines in Bangladesh is their availability and affordability. Traditional remedies are widely accessible in local markets, and their cost is relatively lower compared to modern pharmaceutical drugs. This accessibility is especially significant for the majority of the population who may face economic limitations or

have limited access to mainstream healthcare services.

Traditional remedies have their effect, but they must be administered with prudence and under the supervision of professionals. They have been used for millennia, and some disorders, such as kidney disease, may benefit from them. However, their efficacy and safety may depend on the particular circumstances of each case. Treatment for kidney illness and other medical issues in Bangladesh can be improved by combining contemporary healthcare practices such as consulting a doctor and getting suitable diagnostics with traditional practices like herbal remedies.

Conclusions

Bangladesh's traditional medicines have been used for centuries to treat various ailments, including kidney diseases. Traditional medicines are a crucial part of Bangladesh's healthcare system, as they are accessible and affordable to the majority of the population.

Kidney diseases are a growing health concern in Bangladesh, with high rates of diabetes and hypertension contributing to the problem. Traditional medicines have been used to treat kidney diseases in Bangladesh, and recent research has focused on their efficacy and potential mechanisms of action.

In contrast, plants and their bioactive molecules offer nephroprotective effects, acting as antioxidants, anti-inflammatories, antibiotics, anti-cancer, and diuretics, among other effects. The reviewed works undoubtedly support the use of plants and their bioactive molecules to mitigate risk factors and drug-induced kidney injuries. Furthermore, these results provide a better understanding of how plants act as molecular modulators to alleviate pre-renal and post-renal disorders that indirectly or subsequently can lead to the development of intrinsic kidney disease. Indirect nephroprotective effects have been demonstrated from a wide diversity of plants, including all parts (roots, herbs, leaves, flowers, fruits, and seeds), as well as their by-products such as medicinal plant residue, fruit peels, and pulps. Likewise, therapeutic effects were reported from raw materials, crude extracts, and purified compounds. A wide range of medications, heavy metals, solvents, pesticides, and NSAIDS are all known as nephrotoxic chemicals, which can induce cell necrosis and kidney injury. The present review has encompassed a broad range of nephrotoxic drugs.

The main perspective that can be highlighted from this review is that it broadens the panel of nephroprotective plants by considering not only plants with intrinsic effects or that can reverse nephrotoxicity, but also plants with beneficial effects on kidney diseases. Overall, traditional medicines in Bangladesh have shown promise for kidney protection. However, further research is needed to fully understand their efficacy and potential mechanisms of action. It is essential to note that traditional medicines should be used under the supervision of a healthcare provider, as they may interact with other medications or have adverse effects on certain individuals.

There are nephroprotective plants that contain critical phytochemical ingredients for treating kidney disease. Many herbs have been shown to have nephroprotective characteristics; however, this isn't accurate. While many herbs have been found to have this characteristic, there is a minority that isn't. These plants' effectiveness and safety must be thoroughly investigated by different tests to find out the specific molecules or bioactive compounds which can cure the diseases. Nevertheless, further research is needed to determine the safety and efficacy of these plants for treating kidney-related diseases in humans. It is also important to consider potential side effects and interactions with other medications before using these plants for medicinal purposes.

Therefore, while the kidney-protecting plants of Bangladesh have shown promising results in preliminary studies, more research is needed to fully understand their potential as traditional medicines for kidney health. By continuing to explore the protective properties of plants on renal function, we can pave the way for innovative strategies in preserving kidney health and improving the quality of life for countless individuals. However, it is essential to strike a balance between traditional practices and evidence-based modern medicine, emphasizing the need for informed decisions and expert guidance to ensure kidney health remains uncompromised.

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Online supplementary material:
Table S1. Agents and mechanisms of nephrotoxicity.
Table S2. Plants containing protective factors against cisplatin-induced nephrotoxicity.
Table S3. Nephroprotective drugs and their chemical constituents, along with structures.

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