INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Nephroprotective: A Comprehensive Review

Naveen Tripathi*, Dr. Suprabha Devi

Department of Pharmacy, Institute of Technology and Management, Gorakhpur, Uttar Pradesh, India, 273209.

ARTICLE INFO

Published: 27 May 2025
Keywords:
Dialysis, Glomerulonephritis, Nephrotic Syndrome, Chronic Kidney Disease, Acute Kidney Injury, Nephrotoxicity, and Renal Failure
DOI:
10.5281/zenodo.15528332

ABSTRACT

Waste filtration, electrolyte balancing, blood pressure management, hormone generation, and acid-base maintenance are just a few of the vital roles the kidneys play in preserving general health. Nephrotoxicity, which can result in diseases like acute kidney injury (AKI) and chronic kidney disease (CKD), is the term used to describe kidney damage brought on by dangerous substances including medications, chemicals, and poisons. Numerous chemical and pharmaceutical compounds are linked to various kidney illnesses, such as kidney stones, glomerulonephritis, interstitial nephritis, and nephrotic syndrome. ACE inhibitors, diuretics, immunosuppressants, phosphate binders, and erythropoiesis-stimulating medicines are among the drugs used to treat kidney illnesses, depending on the stage and kind of kidney impairment. In order to improve patient outcomes and stop more kidney damage, early diagnosis and treatment are essential. This article lists the main reasons, kidney disease phases and treatment choices, with an emphasis on the effects of nephrotoxins and therapeutic strategies for different renal disorders.

INTRODUCTION

An essential component of the human body, the kidneys are necessary for preserving general health. They are fist-sized, bean-shaped structures that are situated directly below the rib cage on either side of the spine. Nephrons, which are microscopic filtering units, number around a million in each kidney. The main job of the kidneys is to filter blood, eliminating waste, toxins, and extra fluid, which is then expelled from the body as urine. Apart from their filtering function, the kidneys also control vital body processes like:

1. **Electrolyte and fluid balance:** They make sure the body keeps the right amounts of potassium, sodium, and other electrolytes, which are necessary for the normal operation of muscles and nerves.

***Corresponding Author:** Naveen Tripathi
Address: *Department of Pharmacy, Institute of Technology and Management, Gorakhpur, Uttar Pradesh, India, 273209.*
Email ✉: tripathinaveen53@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

2. **Regulating Blood Pressure Regulation:** By controlling fluid balance and releasing hormones like renin, the kidneys aid in blood pressure maintenance.

3. **Hormone creation:** They oversee creating hormones such as calcitriol, an active form of vitamin D that aids in controlling calcium levels, and erythropoietin, which promotes the creation of red blood cells.

4. **Maintaining Acid-Base Balance:** By removing hydrogen ions and reabsorbing bicarbonate, the kidneys assist in keeping the pH of the body within a normal range. [1]

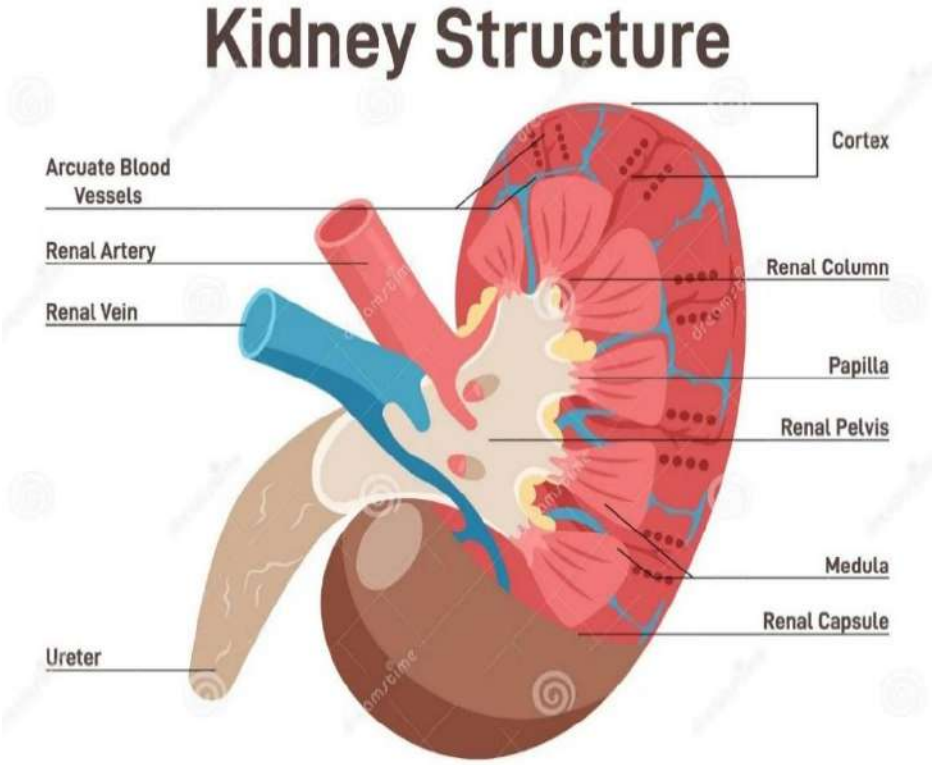

Fig 1. Normal Kidney.

Nephrotoxicity:

The term "nephrotoxicity" describes damage to the kidneys or reduced renal function brought on by exposure to hazardous substances, chemicals, medications, or other factors. It can result in either short-term or long-term renal dysfunction, which impacts the kidneys' capacity to filter waste, maintain fluid and electrolyte balance, and control blood pressure.

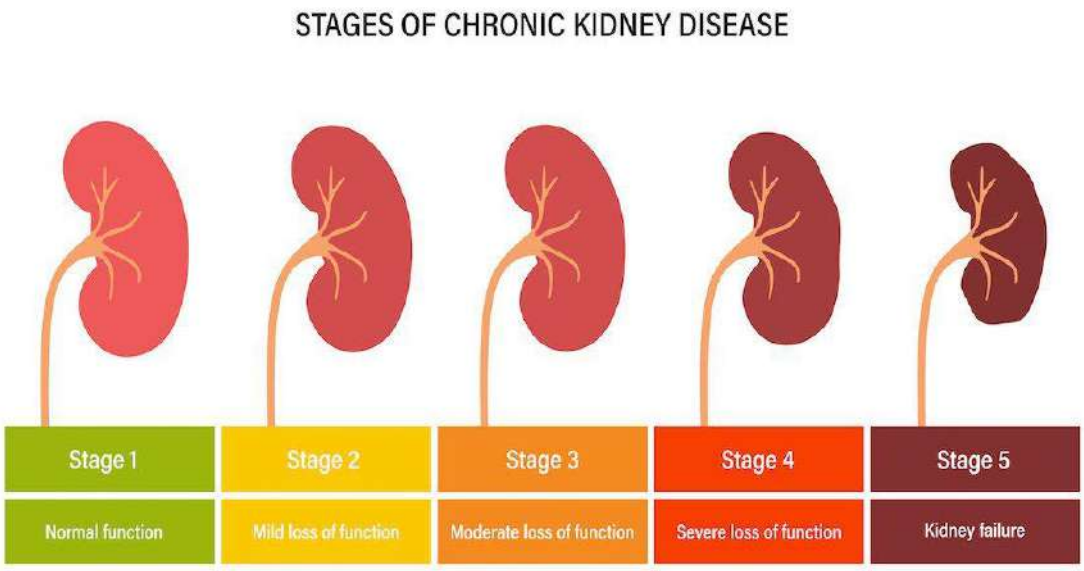

Fig 2. Stages of Chronic Kidney Disease

Chemical And Drug Agent Leads to Different Types of Kidney Disease

Exposure to certain substances, poisons, or medications can cause various kidney disorders. The following is a list of kidney illnesses, along with the chemicals and medications that are known to cause or worsen them:

1. Acute Kidney Injury (AKI)

AKI is a sudden loss of kidney function, often reversible if the cause is removed.

Chemical Agents:

- Ethylene glycol (antifreeze poisoning)
- Heavy metals: Lead, mercury, cadmium, arsenic
- Herbicides: Paraquat
- Toxins: Myoglobin (from rhabdomyolysis), hemoglobin (from hemolysis)

Drug Agents:

- NSAIDs: Ibuprofen, naproxen, ketorolac
- Aminoglycosides: Gentamicin, tobramycin
- Radiocontrast agents: Used in imaging procedures
- Amphotericin B: Antifungal agent
- Cisplatin: Chemotherapy drug
- Acyclovir: Antiviral agent (can cause crystal nephropathy) [2-5]

2. Chronic Kidney Disease (CKD)

CKD is characterized by progressive kidney damage over time.

Chemical Agents:

- Lead and cadmium (chronic exposure)
- Arsenic (in contaminated water)

- Environmental toxins: Persistent organic pollutants

Drug Agents:

- NSAIDs: Long-term use of ibuprofen or naproxen
- Proton Pump Inhibitors (PPIs): Omeprazole, pantoprazole
- Lithium: Used for bipolar disorder
- Herbal remedies: Containing aristolochic acid [6-8]

3. Glomerulonephritis

Inflammation of the glomeruli, often immune-mediated.

Chemical Agents:

- Hydrocarbons: Benzene, toluene (environmental exposure)

Drug Agents:

- Gold salts: Used in rheumatoid arthritis
- Penicillamine: For Wilson's disease or rheumatoid arthritis
- Certain antibiotics: Beta-lactams (e.g., penicillin), sulfonamides [9-10]

4. Interstitial Nephritis

Inflammation of the kidney interstitium, often caused by hypersensitivity reactions.

Drug Agents:

- Antibiotics: Penicillins, cephalosporins, sulfonamides, rifampin
- NSAIDs: Ibuprofen, diclofenac
- Proton Pump Inhibitors (PPIs): Omeprazole, lansoprazole
- Diuretics: Thiazides, furosemide [11-12]

5. Nephrotic Syndrome

Characterized by heavy proteinuria, edema, and hypoalbuminemia.

Chemical Agents:

- Mercury (industrial exposure or contaminated food)

Drug Agents:

- Gold salts: For rheumatoid arthritis
- Penicillamine: For Wilson's disease
- NSAIDs: Rarely [13-14]

6. Tubular Disorders

Damage to the renal tubules, causing problems like Fanconi syndrome or acute tubular necrosis (ATN).

Chemical Agents:

- Heavy metals: Lead, cadmium
- Ethylene glycol: Causes ATN through crystal formation

Drug Agents:

- Aminoglycosides: Gentamicin, tobramycin
- Cisplatin: Chemotherapy drug
- Tenofovir: Antiviral agent
- Ifosfamide: Chemotherapy drug [15-16]

7. Rhabdomyolysis-Induced Kidney Injury

Breakdown of muscle tissue releases myoglobin, causing kidney damage.

Chemical Agents:

- Illicit drugs: Cocaine, amphetamines
- Toxins: Snake venom, severe burns

Drug Agents:

- Statins: At high doses or with drug interactions
- Cocaine: Induces muscle breakdown [17-18]

8. Analgesic Nephropathy

Damage to the kidneys due to chronic use of painkillers.

Drug Agents:

- Combination of NSAIDs and acetaminophen (chronic use) [19]

9. Kidney Stones (Nephrolithiasis)

Crystallization of substances in urine, leading to stones.

Chemical Agents:

- Ethylene glycol: Causes oxalate stones
- High uric acid levels: From lead exposure or gout

Drug Agents:

- Acyclovir: Causes crystal nephropathy
- Indinavir: HIV medication that can form stones [20-21]

10. Hypertensive Nephropathy

Kidney damage due to high blood pressure.

Chemical Agents:

- Lead exposure: Chronic exposure can worsen hypertension

Drug Agents:

- NSAIDs: Can exacerbate hypertension and kidney damage [22-23]

Treatment Of Different Stage of Kidney Disease

1. For Chronic Kidney Disease (CKD)

- Angiotensin-Converting Enzyme (ACE) Inhibitors or Angiotensin II Receptor Blockers (ARBs):
  - Drugs: Enalapril, Lisinopril, Losartan, Valsartan.
  - Purpose: Control blood pressure, reduce proteinuria, and slow progression of CKD.
- Phosphate Binders:
  - Drugs: Sevelamer, Lanthanum carbonate, Calcium acetate.
  - Purpose: Manage hyperphosphatemia in CKD.
- Erythropoiesis-Stimulating Agents (ESAs):
  - Drugs: Epoetin alfa, Darbepoetin alfa.
  - Purpose: Treat anemia associated with CKD.
- Vitamin D Analogs:
  - Drugs: Calcitriol, Paricalcitol.

- Purpose: Manage secondary hyperparathyroidism. [24-29]

2. For Acute Kidney Injury (AKI)

- Diuretics:
- Drugs: Furosemide (loop diuretics).
- Purpose: Manage fluid overload, though use is controversial.
- Electrolyte Management:
- Drugs: Sodium bicarbonate (for metabolic acidosis), potassium binders like Sodium polystyrene sulfonate.
- Purpose: Correct metabolic disturbances. [30-31]

3. For Glomerular Diseases (e.g., Nephrotic Syndrome, Glomerulonephritis)

- Immunosuppressants:
- Drugs: Prednisone, Mycophenolate mofetil, Cyclophosphamide, Tacrolimus.
- Purpose: Reduce immune-mediated damage.
- Anticoagulants:
- Drugs: Warfarin.
- Purpose: Manage hypercoagulable states in nephrotic syndrome.
- Statins:
- Drugs: Atorvastatin, Rosuvastatin.
- Purpose: Treat dyslipidemia. [32-34]

4. For End-Stage Renal Disease (ESRD) and Dialysis

- Antipruritics (for uremic pruritus):
- Drugs: Gabapentin, Pregabalin.
- Antihypertensives:
- Drugs: Beta-blockers, Calcium channel blockers.
- Purpose: Control blood pressure.
- Iron Supplements:
- Drugs: Intravenous iron sucrose, Ferric carboxymaltose.
- Purpose: Correct iron deficiency anemia. [35-36]

5. For Kidney Stones

- Alkalinizing Agents:
- Drugs: Potassium citrate.
- Purpose: Dissolve certain types of stones (e.g., uric acid stones).
- Pain Relievers:
- Drugs: NSAIDs (e.g., ibuprofen), Acetaminophen.
- Alpha Blockers:
- Drugs: Tamsulosin.
- Purpose: Facilitate passage of stones. [37-39]

6. For Polycystic Kidney Disease (PKD)

- Vasopressin Receptor Antagonists:
- Drugs: Tolvaptan.

- Purpose: Slow progression of cyst growth and CKD. [40]

7. For Infections in the Kidney (e.g., Pyelonephritis)

- Antibiotics:
- Drugs: Ciprofloxacin, Amoxicillin-clavulanate, Trimethoprim-sulfamethoxazole.
- Purpose: Treat bacterial infections. [41]

8. Adjunctive Therapy

- Sodium Bicarbonate:
- Purpose: Treat metabolic acidosis in CKD.
- Antiplatelet Agents:
- Drugs: Aspirin.
- Purpose: Prevent cardiovascular complications. [42-43]

Treatment of Renal Disease:

Plant Derived Natural Products:

1. Phyllanthus niruri (Chanca Piedra)

- Flavonoids, lignans, alkaloids, and tannins are examples of active compounds.
- Mechanism: It has been demonstrated to prevent kidney damage by lowering oxidative stress and inflammation. It is well-known for its diuretic, anti-inflammatory, and antioxidant qualities. Traditional medicine frequently uses it to treat kidney stones and maintain renal function.
- Research: By lowering oxidative stress, apoptosis, and inflammation in kidney tissues, Phyllanthus niruri may be able to lessen renal toxicity brought on by nephrotoxic substances like gentamicin. [44–45]

2. Withania somnifera (Ashwagandha)

- Alkaloids and withanolides are active compounds.
- Mechanism: Ashwagandha's anti-inflammatory and antioxidant qualities help lessen kidney damage brought on by inflammation and free radicals. It could help improve renal blood flow by controlling nitric oxide levels.
- Research: By reducing blood creatinine and BUN levels, Withania somnifera has been demonstrated to enhance renal function and lessen gentamicin-induced nephrotoxicity in animal models. [46–48]

3. Cichorium intybus (Chicory)

- Flavonoids, tannins, alkaloids, and inulin are the active ingredients.
- Mechanism: Chicory helps to preserve renal function and lessen oxidative stress because of its diuretic, anti-inflammatory, and antioxidant properties.
- Research: By minimizing renal damage brought on by harmful substances, studies indicate that Cichorium intybus improves kidney health and lessens the effects of cadmium-induced nephrotoxicity. [49–50]

4. Curcuma longa (Turmeric)

- One of the active ingredients is curcumin, a polyphenolic molecule.
- Mechanism: Curcumin has strong anti-inflammatory and antioxidant properties. It aids in lowering inflammation and oxidative

stress, two factors that frequently lead to nephrotoxicity. Additionally, it has been demonstrated to stop cellular apoptosis and kidney fibrosis.

- Research: By lowering indicators of oxidative stress and enhancing kidney function, Curcuma longa has shown protective benefits in cisplatin-induced nephrotoxicity and lead-induced nephropathy. [51–52]

5. Boswellia serrata (Indian Frankincense)

- The active ingredients are boswellic acids.
- Mechanism: Pro-inflammatory cytokines like TNF-α and IL-6 are known to be inhibited by boswellic acids, which also have anti-inflammatory and antioxidant qualities. It also aids in preventing toxins from harming kidney cells.
- Research: By lowering oxidative stress and renal inflammation, Boswellia serrata can guard against NSAID-induced nephrotoxicity. [53–54]

6. Azadirachta indica (Neem)

- Flavonoids, nimbidin, and azadirachtin are the active ingredients.
- Mechanism: Neem has long been utilized as a cleansing, anti-inflammatory, and antioxidant. It can improve renal healing processes and lessen oxidative damage and inflammation in the kidneys.
- Research: By lowering blood creatinine, urea levels, and kidney histopathological damage, neem extracts have been demonstrated to mitigate diabetic nephropathy and gentamicin-induced nephrotoxicity. [55–56]

7. Silybum marianum (Milk Thistle)

- Active Compounds: Silymarin (a flavonoid complex).
- Mechanism: Silymarin is a potent antioxidant that protects liver and kidney cells from oxidative damage. It helps stabilize cell membranes, regenerate damaged tissues, and reduce inflammation.
- Research: Silybum marianum has shown nephroprotective effects in various animal models, particularly in preventing cisplatin-induced nephrotoxicity, by decreasing oxidative stress and improving kidney function markers. [57-58]

8. Tribulus terrestris (Puncture Vine)

- Alkaloids, steroids, flavonoids, and saponins are examples of active compounds.
- Mechanism: Tribulus terrestris, which is well-known for its diuretic, anti-inflammatory, and antioxidant qualities, protects the kidneys by preventing oxidative damage and preserving renal function.
- Research: By lowering blood creatinine and raising antioxidant levels in the kidneys, Tribulus terrestris can prevent gentamicin-induced nephrotoxicity, according to animal experiments. [59–60]

9. Allium sativum (Garlic)

- Flavonoids, sulfur compounds, and allicin are the active ingredients.
- Mechanism: Garlic's anti-inflammatory and antioxidant qualities are well-known. Additionally, it enhances renal function and lessens oxidative stress in the kidneys.

- Research: Garlic's antioxidant qualities and ability to increase renal blood flow may help reduce drug-induced nephrotoxicity, especially that brought on by gentamicin. [61–62]

10. Ginkgo biloba (Ginkgo)

- Flavonoids and terpenoids (ginkgolides) are active compounds.
- Mechanism: Ginkgo, a potent antioxidant, lowers inflammation and increases circulation, all of which can help shield the kidneys from harm.
- Research: Ginkgo biloba can improve kidney function indicators and lessen oxidative damage by protecting against gentamicin-induced nephrotoxicity, according to animal studies. [63–64]

11. Hibiscus rosa-sinensis (Hibiscus)

- Organic acids, flavonoids, and anthocyanins are examples of active compounds.
- Mechanism: Hibiscus, which is well-known for its anti-inflammatory and antioxidant properties, aids in reducing kidney damage brought on by inflammation and oxidative stress.
- Research shows that Hibiscus rosa-sinensis can lessen the effects of nephrotoxicity caused by ethylene glycol by lowering histopathological damage and serum creatinine. [65–66]

12. Glycyrrhiza glabra (Licorice)

- Triterpenoids, flavonoids, and glycyrrhizin are the active ingredients.
- Mechanism: Strong anti-inflammatory, anti-fibrotic, and antioxidant qualities of licorice help shield kidney tissues against fibrosis and injury.
- Research: In models produced by gentamicin and cisplatin, licorice extracts have demonstrated nephroprotective efficacy against drug-induced nephrotoxicity. [67–68]

13. Glycyrrhiza uralensis (Chinese Licorice)

- Glycyrrhizin, glycyrrhetic acid, and flavonoids are the active ingredients.
- Mechanism: Glycyrrhiza uralensis, which is well-known for its hepatoprotective, antioxidant, and anti-inflammatory qualities, provides defense against kidney damage brought on by inflammation and oxidative stress.
- Research: It has been demonstrated to improve renal function and shield the kidneys from oxidative stress by reducing cyclophosphamide-induced nephrotoxicity. [69–70]

14. Moringa oleifera (Drumstick Tree)

- Vitamins, polyphenols, and flavonoids are examples of active compounds.
- Mechanism: The anti-inflammatory and antioxidant qualities of moringa help shield the kidneys from oxidative stress and pollutants.
- Research: In animal models of diabetic nephropathy and gentamicin-induced nephrotoxicity, Moringa oleifera has demonstrated nephroprotective properties, lowering renal damage and enhancing kidney function. [71–73]

15. Pterocarpus marsupium (Indian Kino Tree)

- Pterocarpin, marsupin, and tannins are the active ingredients.
- Mechanism: This plant, which is well-known for its anti-inflammatory and antioxidant properties, aids in shielding the kidneys from harm caused by free radicals.
- Research: By lowering oxidative stress and kidney damage, Pterocarpus marsupium can guard against cisplatin-induced nephrotoxicity. [74–76]

Semi Synthetic Products for Nephrotoxicity:

1. Acetaminophen (Paracetamol) Derivatives

- Compound Semi-Synthetic: N-acetylcysteine (NAC)
- Mechanism: The amino acid cysteine is the semi-synthetic precursor of NAC. It serves as a precursor to glutathione, a potent antioxidant that aids in the kidneys' detoxification of reactive oxygen species (ROS). By restoring glutathione levels and halting oxidative damage, NAC is used therapeutically to treat acute kidney injury (AKI) and acetaminophen-induced nephrotoxicity.
- Research: According to a number of studies, NAC can help lessen kidney damage brought on by nephrotoxic medications like gentamicin and cisplatin. [77–78]

2. Doxorubicin Derivatives

- Doxorubicin (Doxil), a semi-synthetic compound, is liposomal
- Mechanism: A modified form of doxorubicin, liposomal doxorubicin is encapsulated in liposomes to increase its therapeutic index and lessen nephrotoxicity. Liposomal formulations prevent harm to non-target organs, such as the kidneys, while assisting in the drug's targeting of cancer cells.
- Research: Compared to standard doxorubicin, which is known to cause nephrotoxicity, liposomal doxorubicin has demonstrated less renal toxicity. [79–80]

3. Penicillin Derivatives

- Amoxicillin and ampicillin are semi-synthetic compounds.
- Mechanism: Semi-synthetic derivatives of penicillin, ampicillin and amoxicillin have altered side chains that contribute to their broader range of activity. These semi-synthetic antibiotics have a reduced nephrotoxic profile and are less likely to harm kidneys when used in clinical settings, even though penicillin itself can result in drug-induced nephrotoxicity.
- Research: When compared to previous penicillin derivatives, studies have shown that amoxicillin has a superior safety profile with less nephrotoxicity. [81–82]

4. Corticosteroid Derivatives

- Prednisolone/Methylprednisolone is a semi-synthetic compound.
- The mechanism Semi-synthetic corticosteroids prednisolone and methylprednisolone have altered structures that lessen the nephrotoxic adverse effects of natural corticosteroids. Nephrotic syndrome, glomerulonephritis, and autoimmune kidney disorders can all be effectively treated with these medications' strong anti-inflammatory and immunosuppressive properties.

- Research: These corticosteroids lessen nephrotoxic damage in lupus nephritis and nephrotic syndrome and aid in the management of inflammatory kidney illnesses. [83–84]

5. Cisplatin Derivatives

- Nedaplatin is a semi-synthetic platinum-based chemotherapeutic drug that has been chemically altered to lessen nephrotoxicity in comparison to cisplatin. It is utilized as a substitute for cisplatin in cancer treatment because of its better pharmacokinetic characteristics.

- Research: Nedaplatin is a viable treatment option for cisplatin-induced nephrotoxicity, as evidenced by animal studies that indicate it produces reduced renal toxicity. [85–86]

6. Taxane Derivatives

- Semi-Synthetic Substance: Paclitaxel/Docetaxel

- Mechanism: Taxol, a naturally occurring substance obtained from the Pacific yew tree, is the semi-synthetic precursor to docetaxel and paclitaxel. These substances are used to treat a variety of malignancies as chemotherapy drugs. Compared to natural taxol, they are altered to increase stability, bioavailability, and efficacy while lowering nephrotoxic adverse effects.

- Research: Studies indicate that paclitaxel and docetaxel are safer for long-term usage in the treatment of cancer and less nephrotoxic than their natural equivalents. [87–88]

7. Quinine Derivatives

- Chloroquine/hydroxychloroquine is a semi-synthetic compound. Its mechanism These are altered forms of quinine, an alkaloid that is taken from the bark of the cinchona plant and used to treat malaria. In addition to being used to treat autoimmune disorders including rheumatoid arthritis and lupus nephritis, hydroxychloroquine and chloroquine have also been demonstrated to lessen nephrotoxicity in specific circumstances.

- The semi-synthetic derivatives of quinine, chloroquine and hydroxychloroquine, have a safer profile with fewer kidney-related adverse effects, despite quinine's potential for nephrotoxicity. [89–90]

8. Herbal Derivatives

- Semi-Synthetic Substance: Derivatives of Berberine

- Mechanism: To improve its bioavailability and effectiveness in treating renal illnesses, berberine, an alkaloid obtained from a variety of plants, has undergone chemical modification. Its anti-inflammatory, anti-fibrotic, and antioxidant qualities help stop kidney damage and slow the course of chronic kidney disease (CKD).

- Research: By lowering oxidative stress, fibrosis, and inflammation, berberine derivatives have been found to protect against diabetic nephropathy and induced nephrotoxicity. [91–92]

9. Flavonoid Derivatives

- Semi-Synthetic Substance: Derivatives of Rutin and Quercetin

- The mechanism Plant-derived flavonoids quercetin and rutin have undergone chemical

modification to increase their kidney protective properties. These substances can lessen kidney damage brought on by nephrotoxic drugs like gentamicin and cisplatin because of their strong anti-inflammatory, anti-apoptotic, and antioxidant properties.

- Research: Studies have shown that derivatives of rutin and quercetin have nephroprotective properties, enhancing kidney function in nephrotoxic situations. [93–94]

10. Glycoside Derivatives

- Semi-Synthetic Substance: Digoxin and other cardiac glycosides
- Mechanism: Heart failure and arrhythmias are treated with digoxin, a semi-synthetic derivative of the cardiac glycoside ouabain. By improving renal blood flow and lowering glomerular damage, it has demonstrated possible nephroprotective benefits in some mice, while being mostly utilized in cardiovascular treatment.
- Research: Digoxin may enhance renal perfusion and function, particularly when heart failure is the cause of kidney injury. [95–96]

Synthetic Products for Nephrotoxicity

1. Angiotensin-Converting Enzyme (ACE) Inhibitors

- For instance, Ramipril, Lisinopril, and Enalapril
- Mechanism: Angiotensin I is converted to angiotensin II, a peptide that constricts blood vessels and encourages kidney injury, by ACE inhibitors. ACE inhibitors lower blood pressure, glomerular pressure, and proteinuria by blocking this route. These parameters are important in diabetic nephropathy and other types of chronic kidney disease (CKD).
- Research: By enhancing renal function and lowering glomerular hypertension and glomerulosclerosis, ACE inhibitors have been demonstrated in studies to slow the course of kidney disease.

2. Angiotensin II Receptor Blockers (ARBs)

- For instance, Irbesartan, Valsartan, and Losartan
- Mechanism: Like ACE inhibitors, ARBs prevent angiotensin II from acting at its receptor location without interfering with the ACE enzyme. This helps prevent diabetic nephropathy, hypertensive nephropathy, and glomerulonephritis by lowering kidney vasoconstriction, salt retention, and fibrosis.
- Research: Studies have shown that ARBs, especially in people with diabetes and hypertension, are useful in lowering proteinuria and slowing the course of CKD.

3. Statins

- For instance, Rosuvastatin, Simvastatin, and Atorvastatin
- Mechanism: The HMG-CoA reductase enzyme is inhibited by statins, which are medications that decrease cholesterol. Statins have been shown to have anti-inflammatory and antioxidant properties in addition to their ability to lower cholesterol. These properties may help shield the kidneys from harm caused by hyperlipidemia and diabetic nephropathy.
- Research: Statins have been shown to lower proteinuria, maintain kidney function, and

decrease the development of renal fibrosis and diabetic nephropathy.

4. Phosphodiesterase Type 5 (PDE5) Inhibitors

- For instance, Vardenafil, Tadalafil, and Sildenafil
- Mechanism: Although PDE5 inhibitors are mostly used to treat erectile dysfunction, they also increase renal blood flow through vasodilatory effects. By raising cyclic GMP levels, they can enhance glomerular filtration and lessen kidney damage brought on by diabetes and high blood pressure.
- Research: PDE5 inhibitors are promising options for treating nephrotoxicity since preclinical and clinical trials have demonstrated that they may help lessen renal fibrosis, glomerular hypertension, and tubulointerstitial fibrosis.

5. Endothelin Receptor Antagonists

- Bosentan and Ambrisentan, for instance
- Mechanism: Endothelin-1, a strong vasoconstrictor that can result in renal fibrosis and glomerular damage, is inhibited by endothelin receptor antagonists. These medications can lower glomerular hypertension and stop the progression of renal fibrosis by inhibiting endothelin receptors.
- Research: Preclinical and clinical research have indicated that these medications may help lessen kidney damage in diseases such as polyarteritis nodosa, diabetic nephropathy, and hypertensive nephropathy.

6. Selective Serotonin Reuptake Inhibitors (SSRIs)

- For instance, the mechanisms of sertraline, fluoxetine, and paroxetine have been demonstrated to have nephroprotective benefits by lowering oxidative stress, inflammation, and kidney tissue fibrosis, while being generally used for depression and anxiety.
- Research: The potential of SSRIs to lessen tubulointerstitial fibrosis and diabetic nephropathy has been investigated. They could also assist CKD patients in reducing their proteinuria.

7. Metformin

- Mechanism: A biguanide called metformin is used to treat type 2 diabetes. By increasing insulin sensitivity and reducing hepatic glucose synthesis, it lowers blood sugar levels. It has been demonstrated that metformin lowers the risk of diabetic nephropathy and increases glomerular filtration rate (GFR) in diabetic individuals.
- Research: Metformin has demonstrated nephroprotective benefits when administered judiciously in individuals with early-stage diabetic nephropathy, despite concerns over the possibility of lactic acidosis in cases of severe renal impairment.

8. SGLT2 Inhibitors (Sodium-Glucose Cotransporter 2 Inhibitors)

- For instance, empagliflozin, dapagliflozin, and canagliflozin
- Mechanism: SGLT2 inhibitors assist reduce blood glucose levels by blocking the kidneys' ability to reabsorb glucose. By lowering glomerular hyperfiltration, enhancing renal function, and lowering albuminuria, these medications also directly protect the kidneys.

- Research: SGLT2 inhibitors have been shown in clinical trials to considerably slow the evolution of diabetic nephropathy, lower proteinuria, and postpone the need for dialysis in diabetic patients.

9. Corticosteroids (Synthetic)

- For instance, methylprednisolone and prednisolone
- Mechanism: Anti-inflammatory and immunosuppressive medications called synthetic corticosteroids are used to treat inflammatory kidney disorders and autoimmune illnesses. Particularly in diseases like glomerulonephritis, lupus nephritis, and nephrotic syndrome, they aid in lowering inflammation and immune-mediated kidney damage.
- Research: Methylprednisolone and prednisolone work well to avoid kidney damage from autoimmune disorders and to treat inflammatory kidney illnesses.

10. Cilastatin

- Mechanism: The synthetic drug cilastatin is used in conjunction with the broad-spectrum antibiotic imipenem. Cilastatin reduces imipenem's nephrotoxicity by blocking the renal enzyme dehydropeptidase-1, which stops imipenem from being broken down in the kidneys.
- Research: When treating infections with imipenem, especially in individuals with renal impairment, cilastatin is utilized to avoid renal damage.

11. Carbapenem Derivatives

- For instance, Ertapenem and Meropenem
- Mechanism: Compared to more traditional antibiotics like gentamicin and amikacin, these synthetic broad-spectrum antibiotics have a lesser nephrotoxic profile because of their modified carbapenem structure.
- Research: Studies have indicated that carbapenem derivatives, particularly meropenem, are less likely to cause nephrotoxicity and have a safer renal profile.

12. N-acetylcysteine (NAC)

- Mechanism: Acetaminophen-induced liver damage is countered by NAC, a synthetic derivative of the amino acid cysteine. Because of its antioxidant qualities, NAC guards against oxidative stress, a major contributing factor to drug-induced nephrotoxicity.
- Research: The nephroprotective properties of NAC are extensively investigated, especially in individuals receiving chemotherapy or gentamicin or other nephrotoxic medicines. [97–106]

REFERENCES

1. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).
2. "Ethylene Glycol Toxicity: A Review of Management and Outcomes." American Journal of Kidney Diseases, 2008.
3. "Heavy Metal Toxicity and Kidney Injury." Environmental Toxicology and Pharmacology, 2012.
4. Nephrotoxicity of Aminoglycosides: Mechanisms and Prevention." The Journal of Clinical Pharmacology, 2013.
5. "Nonsteroidal Anti-inflammatory Drugs and the Kidney." Journal of the American Society of Nephrology, 2004.

6. Chronic Kidney Disease and Environmental Toxins: The Role of Lead and Cadmium." American Journal of Kidney Diseases, 2010.
7. "Chronic Use of NSAIDs and Risk of Kidney Disease." Clinical Journal of the American Society of Nephrology, 2010.
8. Proton Pump Inhibitors and Kidney Disease: A Review of the Evidence." American Journal of Kidney Diseases, 2016.
9. "Toluene and Benzene Exposure and Kidney Disease: A Review of the Literature." Environmental Health Perspectives, 2013.
10. "Drug-Induced Glomerulonephritis: The Role of Gold and Penicillamine." Journal of Nephrology, 2008.
11. "Drug-Induced Interstitial Nephritis: A Review of Antibiotic-induced Cases." Kidney International, 2009.
12. "NSAIDs and Renal Effects: Mechanisms and Prevention." Nephrology Dialysis Transplantation, 2011.
13. "Mercury Exposure and Kidney Disease: A Review." Environmental Toxicology and Pharmacology, 2015.
14. "Drug-induced Nephrotic Syndrome: The Role of Gold and Penicillamine." Clinical Nephrology, 2006.
15. "Heavy Metals and Kidney Disease: An Overview." Kidney International, 2007.
16. "Nephrotoxicity of Aminoglycosides and Cisplatin." American Journal of Kidney Diseases, 2012.
17. "Rhabdomyolysis and Acute Kidney Injury: Role of Illicit Drugs." Nephrology Dialysis Transplantation, 2011.
18. "Statin-Induced Myopathy and Kidney Injury." Kidney International, 2009.
19. "Chronic Use of Painkillers and Renal Function: A Review of Analgesic Nephropathy." Kidney International, 2010.
20. Ethylene Glycol and Oxalate Stone Formation." Urological Research, 2006.
21. "Crystal Nephropathy Induced by Acyclovir and Indinavir." Journal of Clinical Pharmacology, 2005.
22. "Lead and Kidney Disease: Mechanisms of Hypertensive Nephropathy." Nephrology Dialysis Transplantation, 2014.
23. "The Role of NSAIDs in Hypertension and Kidney Disease." Hypertension Research, 2013.
24. Effect of Angiotensin-Converting Enzyme Inhibitors on the Progression of Chronic Kidney Disease: A Meta-analysis. Journal of the American Society of Nephrology. 2013.
25. A Meta-analysis of the Effects of Angiotensin Receptor Blockers on Proteinuria in Chronic Kidney Disease. Kidney International. 2014.
26. A Randomized Trial of Sevelamer in Chronic Kidney Disease. New England Journal of Medicine. 2009.
27. Phosphate Binders in Chronic Kidney Disease: Review of Efficacy and Safety. Kidney International Supplements. 2017.
28. Use of Erythropoiesis-Stimulating Agents in Chronic Kidney Disease. American Journal of Kidney Diseases. 2013.
29. Vitamin D in Chronic Kidney Disease: A Review. American Journal of Kidney Diseases. 2011.
30. Diuretics in Acute Kidney Injury: A Systematic Review. American Journal of Kidney Diseases. 2014.
31. Sodium Bicarbonate in Acute Kidney Injury. Nephron Clinical Practice. 2009.
32. Immunosuppressive Treatment in Glomerulonephritis. Kidney International. 2009.
33. Hypercoagulability in Nephrotic Syndrome: A Review of the Literature. Seminars in Thrombosis and Hemostasis. 2012.
34. Statin Use in Chronic Kidney Disease: An Overview. Journal of the American College of Cardiology. 2009.

35. Gabapentin in the Treatment of Uremic Pruritus in Dialysis Patients. Nephrology Dialysis Transplantation. 2005.
36. Iron Therapy in Chronic Kidney Disease: A Comprehensive Review. Kidney International. 2013.
37. Potassium Citrate in the Treatment of Kidney Stones: A Review of Literature. Urological Research. 2008.
38. Nonsteroidal Anti-inflammatory Drugs in Kidney Stones: Efficacy and Safety. Urology Journal. 2012.
39. The Role of Alpha-Blockers in the Treatment of Ureteral Stones. Journal of Urology. 2007.
40. Tolvaptan in Autosomal Dominant Polycystic Kidney Disease. New England Journal of Medicine. 2012.
41. Antibiotics for Urinary Tract Infections in Adults: Current Practice and New Approaches. The Lancet Infectious Diseases. 2015.
42. Treatment of Metabolic Acidosis in Chronic Kidney Disease: Current and Future Perspectives. Clinical Journal of the American Society of Nephrology. 2010.
43. The Role of Aspirin in Cardiovascular Risk Reduction in Chronic Kidney Disease. Nephrology Dialysis Transplantation. 2013.
44. Adebayo JO, Adesokan AA, Olatunji LA, Buoro DO, Soladoye AO. Effect of ethanolic extract of Phyllanthus amarus on serum lipid profile and kidney function in rats. J Ethnopharmacol. 2005;100(1-2):123-126.
45. Jain A, Katewa S, Galav P, Nag A. Evaluation of nephroprotective activity of the methanolic extract of Phyllanthus niruri in gentamicin-induced nephrotoxicity in rats. J Herb Med. 2015;5(3):147-151.
46. Jeyanthi GP, Subramanian P. Nephroprotective effect of Withania somnifera: A dose-dependent study using biochemical and histopathological analysis. Indian J Exp Biol. 2010;48(11):1115-1121.
47. Jeyanthi GP, Subramanian P. Influence of Withania somnifera on lipid peroxidation and antioxidant status in gentamicin-induced nephrotoxic rats. Mol Cell Biochem. 2010;335(1-2):61-67.
48. Govindappa M, Chandrappa CP, Lokesh S, Chandrasekhar N, Ajaykumar K. Protective effect of Withania somnifera against gentamicin-induced nephrotoxicity in rats. Braz J Pharmacogn. 2019;29(1):88-94.
49. Zaki SM, Ashour AA, Elshazly SA, Soliman MM, Soliman MA. Protective effect of chicory and/or artichoke leaves extracts on chronic nephrotoxicity induced by carbon tetrachloride and gamma-irradiation in rats. J Biochem Mol Toxicol. 2021;35(12)
50. Khaki A, Khaki AA, Hajhosseini L, Golzar FS, Ainehchi N. Beneficial effects of Cichorium intybus L. extract on oxidative status and spermatogenesis in male rats. J Med Plants Res. 2013;7(10):664-669.
51. Sahu BD, Kuncha M, Sindhura GJ, et al. The renoprotective effect of curcumin in cisplatin-induced nephrotoxicity. J Exp Pharmacol. 2011;3:171-180.
52. Ramesh G, Reeves WB. In vitro and in vivo renal tubular cytoprotection by curcumin in cisplatin-induced renal epithelial cell apoptosis. Arch Toxicol. 2007;81(6):405-413.
53. Abdel-Salam OM, Khadrawy YA, El-Shamarka ME, et al. Effects of Boswellia serrata resin extract on acute inflammation in rats. Sci Pharm. 2011;79(4):987-999.
54. Gayathri B, Manjula N, Vinaykumar KS, et al. Pure compound from Boswellia serrata extract exhibits anti-inflammatory property in human PBMCs and mouse macrophages through inhibition of TNFα, IL-1β, NO and MAP kinases. Int Immunopharmacol. 2007;7(4):473-482.
55. Bhanwra S, Singh J, Khosla P. Effect of Azadirachta indica (Neem) leaf aqueous

extract on paracetamol-induced liver damage in rats. Indian J Physiol Pharmacol. 2000;44(1):64-68.
56. Chattopadhyay RR. Possible mechanism of hepatoprotective activity of Azadirachta indica leaf extract: part II. J Ethnopharmacol. 2003;89(2-3):217-219.
57. Soto C, Recoba R, Barrón H, et al. Silymarin increases antioxidant enzymes in alloxan-induced diabetes in rat pancreas. Comp Biochem Physiol C Toxicol Pharmacol. 2003;136(3):205-212.
58. Pradeep K, Mohan CV, Gobianand K, et al. Silymarin modulates the oxidant-antioxidant imbalance during diethylnitrosamine induced oxidative stress in rats. Eur J Pharmacol. 2007;560(2-3):110-116.
59. Kumar S, Kumar V, Prakash O. Antidiabetic and hypolipidemic activities of Tribulus terrestris (Linn.) fruit extract in streptozotocin induced diabetic rats. J Complement Integr Med. 2011;8(1):Article 13.
60. Adaay MH, Elhassani AK. Antibacterial activity of Tribulus terrestris L. extracts against pathogenic bacteria isolated from patients with burns infection. J Nat Sci Res. 2013;3(8):94-99.
61. Banerjee SK, Maulik SK. Effect of garlic on cardiovascular disorders: a review. Nutr J. 2002;1:4.
62. El-Demerdash FM, Yousef MI, El-Naga NI. Biochemical study on the hypoglycemic effects of onion and garlic in alloxan-induced diabetic rats. Food Chem Toxicol. 2005;43(1):57-63.
63. Smith JV, Luo Y. Studies on molecular mechanisms of Ginkgo biloba extract. Appl Microbiol Biotechnol. 2004;64(4):465-472.
64. DeFeudis FV, Drieu K. Ginkgo biloba extract (EGb 761) and CNS functions: basic studies and clinical applications. Curr Drug Targets. 2000;1(1):25-58.
65. Sachdewa A, Khemani LD. Effect of Hibiscus rosa-sinensis Linn. ethanol flower extract on blood glucose and lipid profile in streptozotocin induced diabetes in rats. J Ethnopharmacol. 2003;89(1):61-66.
66. Obouayeba AP, Diarrassouba M, Soumahin EF, et al. Phytochemical analysis, purification and identification of Hibiscus anthocyanins. J Pharm Chem Biol Sci. 2014;2(2):87-96.
67. Asl MN, Hosseinzadeh H. Review of pharmacological effects of Glycyrrhiza sp. and its bioactive compounds. Phytother Res. 2008;22(6):709-724.
68. Fiore C, Eisenhut M, Krausse R, et al. Antiviral effects of Glycyrrhiza species. Phytother Res. 2008;22(2):141-148.
69. Wang ZY, Nixon DW. Licorice and cancer. Nutr Cancer. 2001;39(1):1-11.
70. Tang ZH, Chen X, Wang ZY, et al. Pharmacokinetics of glycyrrhizin and its metabolites in rats. Biopharm Drug Dispos. 2009;30(2):77-90.
71. Akinrinde AS, Adebiyi OE, Adefisayo MA, et al. Nephroprotective effect of methanol extract of Moringa oleifera leaves in renal ischemia-reperfusion injury in rats. J Integr Med. 2021;19(1):42-49.
72. Altaee AH, Fadheel WS. The nephroprotective effects of Moringa oleifera extract against iodinated contrast-induced nephrotoxicity in male rats. J Pharm Res Int. 2019;28(6):1-9.
73. Abdel-Latif MA, Khalil RH. Assessment of hepatoprotective, nephroprotective efficacy, and oxidative stress responses to dietary Moringa oleifera leaf extract in Nile tilapia (Oreochromis niloticus) exposed to sub-chronic sodium fluoride. Food Sci Nutr. 2021;9(10):5584-5594.
74. Gupta P, Yadav DK, Siripurapu RK, Palit G, Maurya R. Nephroprotective role of alcoholic extract of Pterocarpus marsupium heartwood against experimentally induced diabetic

nephropathy in rats. Pharm Biol. 2016;54(10):2243-2251. doi:10.3109/13880209.2016.1153665.

75. Kumar A, Nair V, Singh S, Gupta YK. Evaluation of anti-diabetic and anti-oxidative activity of Pterocarpus marsupium in experimental models. Indian J Clin Biochem. 2010;25(1):67-74.
76. Muthenna P, Akileshwari C, Reddy GB. Pterocarpus marsupium extract inhibits aldose reductase and advanced glycation end products in vitro: a possible therapy for diabetic complications. Phytother Res. 2012;26(7):1022-1027. doi:10.1002/ptr.3693.
77. Prescott LF, Illingworth RN, Critchley JA, et al. Intravenous N-acetylcysteine: the treatment of choice for paracetamol poisoning. BMJ. 1979;2(6198):1097-1100. doi:10.1136/bmj.2.6198.1097.
78. Liu Y, Liu JP, Xia Y. N-acetylcysteine for adults with acute kidney injury. Cochrane Database Syst Rev. 2020;2(2):CD007078.
79. Batist G, Barton J, Chaikin P, et al. Myocet (liposome-encapsulated doxorubicin citrate): a review of the pharmacology, pharmacokinetics, and clinical experience. Clin Breast Cancer. 2002;3(Suppl 2):S22-S28.
80. Gabizon A, Shmeeda H, Barenholz Y. Pharmacokinetics of pegylated liposomal Doxorubicin. Clin Pharmacokinet. 2003;42(5):419-436.
81. Kaye CM, Allen A, Poyser RH, et al. The clinical pharmacokinetics of amoxycillin. Clin Pharmacokinet. 1982;7(4):282-319.
82. Rodríguez-Baño J, Navarro MD, Retamar P, et al. β-lactam/β-lactam inhibitor combinations for serious infections caused by extended-spectrum β-lactamase-producing Enterobacteriaceae: a meta-analysis. Lancet Infect Dis. 2012;12(4):313-326.
83. Bolton WK, Remuzzi G, Heerspink HJL, et al. Effect of fostamatinib on kidney inflammation and fibrosis: Results from the fostamatinib for proteinuria due to diabetic nephropathy (FORTRESS) trial. Diabetes Care. 2020;43(10):2528-2535.
84. Bomback AS, Canetta PA, Beck LH, et al. Treatment of primary membranous nephropathy with rituximab: a systematic review. Clin J Am Soc Nephrol. 2009;4(4):734-744.
85. Arakawa T, Nakajima K, Iwashina M, et al. Comparative nephrotoxicity of cisplatin and nedaplatin in patients with head and neck cancer. J Int Med Res. 2020;48(5):300060520920464.
86. Yamamoto N, Nakagawa K, Nishimura Y, et al. Phase I study of nedaplatin and concurrent thoracic radiotherapy in patients with unresectable, locally advanced, non-small-cell lung cancer. J Clin Oncol. 2003;21(20):3835-3841.
87. Markman M. Liposomal formulations of anthracyclines: clinical utility in the treatment of cancer. Oncologist. 1999;4(2):87-92.
88. Rowinsky EK, Donehower RC. The clinical pharmacology of paclitaxel (Taxol). Semin Oncol. 1993;20(4 Suppl 3):16-25.
89. Schrezenmeier E, Dörner T. Mechanisms of action of hydroxychloroquine and chloroquine: implications for rheumatology. Nat Rev Rheumatol. 2020;16(3):155-166.
90. Mackenzie AH. Dose refinements in long-term therapy of rheumatoid arthritis with antimalarials. Am J Med. 1983;75(1A):40-45.
91. Zuo L, Zhou T, Pannell BK, et al. Berberine for kidney disease: A review of molecular mechanisms. Biomed Pharmacother. 2022;147:112671.
92. Li Z, Guo X, Huang X, et al. Protective effects of berberine on cisplatin-induced nephrotoxicity via anti-apoptotic and anti-inflammatory mechanisms in mice. Oncotarget. 2017;8(58):101567-101575.

93. Oteiza PI, Fraga CG, Galleano M. Quercetin and rutin as potential modifiers of oxidative stress in chronic diseases. Oxid Med Cell Longev. 2021;2021:6646921.
94. Boots AW, Haenen GR, Bast A. Health effects of quercetin: from antioxidant to nutraceutical. Eur J Pharmacol. 2008;585(2-3):325-337.
95. Hauptman PJ, Kelly RA. Digitalis. Circulation. 1999;99(9):1265-1270.
96. Gheorghiade M, Ferguson D. Digoxin: a neurohormonal modulator in heart failure? Circulation. 1991;84(5):2181-2186.
97. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. N Engl J Med. 1993;329(20):1456-1462.
98. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med. 2001;345(12):861-869.
99. Tonelli M, Moye L, Sacks FM, Kiberd B, Curhan G. Pravastatin for secondary prevention of cardiovascular events in persons with mild chronic renal insufficiency. Ann Intern Med. 2003;138(2):98-104.
100. Wanner C, Inzucchi SE, Lachin JM, et al. Empagliflozin and progression of kidney disease in type 2 diabetes. N Engl J Med. 2016;375(4):323-334.
101. Tepel M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D, Zidek W. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. N Engl J Med. 2000;343(3):180-184.
102. Batist G, Gelmon KA, Chi KN, et al. Safety, pharmacokinetics, and efficacy of CPX-351 in patients with advanced solid tumors. Clin Cancer Res. 2015;21(4):985-992.
103. Himmelfarb J, Tuttle KR. New therapies for diabetic kidney disease. N Engl J Med. 2013;369(26):2549-2550.
104. Rauen T, Eitner F, Fitzner C, et al. Intensive supportive care plus immunosuppression in IgA nephropathy. N Engl J Med. 2015;373(23):2225-2236.
105. Ruggenenti P, Perna A, Remuzzi G. Retarding progression of chronic renal disease: the neglected promise of ACE inhibitors. BMJ. 2001;322(7277):368-372.
106. Pitt B, Bakris G, Ruilope LM, DiCarlo L, Mukherjee R. Serum potassium and clinical outcomes in the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS). Circulation. 2008;118(16):1643-1650.

HOW TO CITE: Naveen Tripathi*, Dr. Suprabha Devi, Nephroprotective: A Comprehensive Review, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 5, 4409-4427. https://doi.org/10.5281/zenodo.15528332