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ROLE OF PANTS AS NEPHROPROTECTIVE AGENTS – A REVIEW

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ABSTRACT

Plants have always played a vital role in the life of man in the form of food and medicine. In Ayurveda there is a remedy for every disorder using some parts of plants. Many plants have provided a vital source of potentially useful new compounds for the development of effective therapy to combat a variety of problems. Nephrotoxicity is one of the most common problems of man and usually occurs when the body is exposed to a drug or toxin. A large number of medicinal plants, natural products and dietary components have been evaluated as potential nephroprotective agents. Many plants have been used for the treatment of kidney failure in traditional system of medicine throughout the world. In this article, an attempt has been made to gather every possible information about the plants which have shown nephroprotetive properties which will be a ready reference for future researchers.

KEYWORDS: Ayurveda, Nephrotoxicity, Medicinal plants, kidney, Gentamycin, cisplatin.

INTRODUCTION

Nephrotoxicity is the most common kidney problems and occurs when body is exposed to a drug or toxin. When kidney damage occurs, body unable to ride off excess urine and wastes from the body and blood electrolytes (such as potassium and magnesium) will become elevated. Nephrotoxicity is manifested functionally by decreased urine concentrating capacity, tubular proteinuria, lysosomal enzymuria and mid glucosuria, decreased ammonium excretion lowering of glomerular filtration rate, creatinine clearance and increase in serum BUN (blood urea nitrogen), serum creatinine level with kidney tissue morphological alteration.

Risk factors for nephrotoxicity:

- The elderly are more likely to overdose on antibiotics or analgesics.
- Kidneys already weakened by conditions such as diabetes can be particularly susceptible to nephrotoxicity.
- Server dehydration.
- Prolonged exposure to heavy metals or solvents.
- Presence of diseases that cause the overproduction of uric acid.

Symptoms:

- Excess urea in the blood (azotemia).
- Anemia.
- Increased hydrogen ion concentration in the blood (acidosis).
- Excess fluids in the body (over hydration).
- High blood pressure (hypertension).
- Serious symptoms of kidney failure may leads to seizures and coma.

Pathophysiology:

- Drugs produce nephrotoxicity by interfering with renal blood flow, increase in the kidney weight, glomerular function or tubular function.
- Many drugs are nephrotoxic because they are excreted from the body primarily by the kidneys.
- Most nephrotoxic drugs cause proximal renal tubular necrosis.
- If renal injury is severe, acute renal failure develops.[15]

Kidney toxicity induced by nephrotoxic agents:

- **Renal failure:** Renal failure is a common clinical syndrome. It is defined as a rapid decline in

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renal function resulting in abnormal retention of serum creatinine and blood urea which must be excreted. The clinical manifestations of renal failure are the decline in glomerular filtration rate (GFR) and the inability of the kidney to excrete the toxic metabolic substances produced in the body. In addition, there is failure of regulation of fluids and electrolyte balance along with endocrine dysfunction. Depending up on the severity, it is divided as acute and chronic renal failure.[6]

There are two types of renal failure:

1. Acute renal failure.
2. Chronic renal failure.

1. **Acute renal failure (ARF):** It is defined as a significant decline in renal excretory function occurring over hours or days. This is usually detected clinically by arise in the plasma concentration of the urea or creatinine. Acute renal failure may arise as an isolated problem, but much more commonly occurs in the setting of circulatory disturbance associated with severe illness, trauma, or surgery; transient renal dysfunction.

2. **Chronic renal failure (CRF):** It is the clinical syndrome of the metabolic and systemic consequences of a gradual, substantial and irreversible reduction in the excretory and homeostatic functions of the kidneys.[36]

Causes of chronic renal failure:

- The most important causes of chronic kidney disease are diabetes, glomerulo nephritis, hypertension and other vascular disease.
- It can be difficult to recognize because the symptoms and clinical manifestations are non-specific Arteriopathic renal disease and hypertension
- Glomerulonephritis
- Diabetes
- Infective, obstructive and reflux nephropathies
- Congenital disease
- Familial or hereditary kidney disease, e.g. polycystic kidneys
- Hypocalcaemia
- Connective tissue diseases
- Neoplasm's
- Myeloma
- Reflux nephropathy
- Renal bone disease is a major cause of disability in patients with terminal renal failure.
- Drugs causing nephrotoxicity:
- Drugs, diagnostic agents and chemicals are well known to be nephrotoxic. The following are the some of the important nephrotoxic agents. [32][13]

1. **Antibiotics :**
   - Amino glycosides (10-15%incidences of ATN):-Gentamycin, Amikacin, Kanamycin, Streptomycin, Toberamycin, Neomycin.
   - Quinolones: - Ciprofloxacin, Levofloxacin.
   - Others: - Sulfonamides, rifampin, tetracycline, acyclovir, pentamidine, Vancomycin, amphotericin-B.
2. **Chemotherapy and immunosuppressant's :** Cisplastin, methotrexate, mitomycin, Cyclosporine, ifosphamide.
3. **Heavy metals :** Mercury poisoning, lead poisoning, arsenic poisoning, bismuth, Gold, germanium, chromium, lithium.
4. **Anti-hyperlipidemics:-**
   - Statin drugs- rhabdomyolysis
   - Gemfibrozil (associated with ARF)
5. **Miscellaneous: -** Radioactive agents.
6. **NSAIDS: -** Paracetmol, ibuprofen, aspirin, etc.
7. **Drugs of abuse: -** Cocaine, Heroin, Methamphetamine

Nephrotoxic agents can produce damage either by directly reacting with cellular macromolecules and membrane components or from metabolism within the tubular cells to toxic products. The agents which cause direct toxicity are heavy metals like Hg, Pb, which interact with sulfhydryl groups, organic cations such as spermine, cationic amino acids, amino glycosides which interacts with membrane phospholipids, polyene antibiotics like amphotericin-B which interacts with membrane cholesterol. Fluoride and oxalates produced by hepatic metabolism of metabolism of methoxyflurane intermediates of cisplastin, cystine conjugates, cephaloridine and acetaminophen induced damage by their metabolites. These toxic metabolites mainly include free radicals.

The nephrotoxins damage specific segment of the nephron to a greater extent than the other segments. The proximal tubule is the most commonly affected, because of the presences of inducible type of microsomal mixed function

oxidises (cytochrome P 450) which have been

Table 1: List of plants having nephroprotective activity:

Sr. no.	Plant name	Family	Part used	Screening method
1.	Abutilon indicum	Malvaceae	Whole plant	Gentamycin
2.	Acorus calamus	Araceae	Aerial Parts	Acetaminophen
3.	Achyranthes aspera	Amarnthacae	Whole plant	Lead acetate induced
4.	Adhatoda zeylanica	Acanthaceae	Leaves	Gentamycin
5.	Aegle marmelos	Rutaceaeae	Leaves	Gentamycin
6.	Aloe barbadensis	Xanthorrhoeaceae	Leaves	Cisplatin & Gentamycin
7.	Aerva javanica	Amaranthaceae	Fresh roots	Cisplatin
8.	Aerva lanata	Amaranthaceae	Whole plant	Cisplatin
9.	Aerva lanata	Amaranthaceae	Whole plant	Gentamycin
10.	Allium sativum L	Amaryllidaceae	Garlic	Gentamycin
11.	Andrographis paniculata	Acanthaceae	Roots	Gentamycin
12.	Anthoxanthum odoratum	Poaceae	Aerial parts	Acetaminophen
13.	Aristolochia indica	Aristolochiaceae	Leaves	Gentamycin
14.	Avuri kudineer	Fabaceae	Roots and Leaves	Cisplatin
15.	Bauhinia variegatea linn	Caesalpiniaceae	Stems	Cisplatin
16.	Basella alba L.	Basellaceae	Whole plant	Gentamycin
17.	Berberris aristata	Berberidaceae	Root bark	Cisplatin
18.	Bauhinia variegate	Caesalpiniaceae	Stems	Gentamycin
19.	Benincasa hispida	Cucurbitaceae	Fruit	Cisplatin
20.	Boerhaavia diffusa	Nyctaginaceae	Leaves	Cisplatin
21.	Butea monosperma	Fabaceae	Whole plant	Gentamycin
22.	Bridelia retusa	Phyllanthaceae	Bark	Ccl_4
23.	Carica papaya	Caricaceae	Seeds	Cisplatin
24.	Cassia auriculata	Fabaceae	Root	Cisplatin
25.	Cassia auriculata	Fabaceae	Root	Gentamycin
26.	Casuarina equisetifolia	Casuarinaceae	Dried leaves	Gentamycin
27.	Canarium schweinfurthii	Poaceae	Stem bark	Acetaminophen
28.	Ceratonia silique	Fabaceae	Pods and Leaves	Cisplatin
29.	Cichorium intybus	Asteraceae	Aerial Parts	Cisplatin
30.	Cinnamon	Lauraceae	Peel	Gentamycin
31.	Clitoria ternatea	Papilionaceae	Whole plant	APAP-induced
32.	Crataeva nurvula	Capparidaceae	Fruit	Gentamycin
33.	Cucurbita pepo	Cucurbitaceae	Seeds	Cisplatin
34.	Curcuma longa	Zingeberaceae	Rhizome	Cadmium induced
35.	Dichrostachys cinera	Mimosaceae	Roots	Cisplatin
36.	Drynaria fortune	Polypodiaceae	Whole plant	Silver chloride induced
37.	Euphorbia neriifolia	Euphorbiaceae	Leaves	N-nitroso dimethyl amine
38.	Emblica officinalis	Euphorbiaceae	Fruits	Gentamycin
39.	Enicostemma littorale Blume	Gentianaceae	Whole dried plant	Gentamycin
40.	Abutilon indicum	Malvaceae	Whole plant	Gentamycin
41.	Acorus calamus	Araceae	Aerial Parts	Acetaminophen
42.	Achyranthes aspera	Amarnthacae	Whole plant	Lead acetate induced

43.	Adhatoda zeylanica	Acanthaceae	Leaves	Gentamycin
44.	Aegle marmelos	Rutaceaeae	Leaves	Gentamycin
45.	Aloe barbadensis	Xanthorrhoeaceae	Leaves	Cisplatin & Gentamycin
46.	Aerva javanica	Amaranthaceae	Fresh roots	Cisplatin
47.	Aerva lanata	Amaranthaceae	Whole plant	Cisplatin
48.	Aerva lanata	Amaranthaceae	Whole plant	Gentamycin
49.	Allium sativum L	Amaryllidaceae	Garlic	Gentamycin
50.	Andrographis paniculata	Acanthaceae	Roots	Gentamycin
51.	Anthoxanthum odoratum	Poaceae	Aerial parts	Acetaminophen
52.	Aristolochia indica	Aristolochiaceae	Leaves	Gentamycin
53.	Avuri kudineer	Fabaceae	Roots and Leaves	Cisplatin
54.	Bauhinia variegatea linn	Caesalpiniaceae	Stems	Cisplatin
55.	Basella alba L.	Basellaceae	Whole plant	Gentamycin
56.	Berberris aristata	Berberidaceae	Root bark	Cisplatin
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61.	Bridelia retusa	Phyllanthaceae	Bark	Ccl_4
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67.	Ceratonia silique	Fabaceae	Pods and Leaves	Cisplatin
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72.	Cucurbita pepo	Cucurbitaceae	Seeds	Cisplatin
73.	Curcuma longa	Zingeberaceae	Rhizome	Cadmium induced
74.	Dichrostachys cinera	Mimosaceae	Roots	Cisplatin
75.	Drynaria fortune	Polypodiaceae	Whole plant	Silver chloride induced
76.	Euphorbia neriifolia	Euphorbiaceae	Leaves	N-nitroso dimethyl amine
77.	Emblica officinalis	Euphorbiaceae	Fruits	Gentamycin
78.	Enicostemma littorale Blume	Gentianaceae	Whole dried plant	Gentamycin
79.	Eryngium caucasicum	Apiaceae	Aerial Parts	Gentamycin
80.	Pimpinella tirupatiensis	Apiaceae	Whole plant	Acetaminophen
81.	Plectranthus amboinicus	Lamiaceae	Leaves	Acetaminophen
82.	Pongamia pinnata	Papilionaceae	Flowers	Cisplatin
83.	Portula oleracea	Portulaceae	Leaves and stem	Cisplatin
84.	Punicagranatum	Puniaceae	Fruit peel	Ferric nitrilo tri Acetate induced
85.	Psidium guajava L	Myrtaceae	Leaves	Doxorubicin-induced
86.	Pseudocedrela kotschyi	Meliaceae	Root	Alloxan-induced
87.	Rhazya stricta	Apocynaceae	Leaves	Gentamycin
88.	Rubia cardifolia Linn	Rubiaceae	Root	Ethylene glycol
89.	Rubus ellipticus	Rosacea	Fruits	Cisplatin

90.	Salviae radix	Lamiaceae	Whole plant	Cisplatin
91.	Salvia officinalis	Lamiaceae	Leaves	Cisplatin
92.	Sida cordifolia Linn.	Malvacea	Root	Gentamycin
93.	Solanum nigrum	Solanaceae	Whole plant	Amphotericin B
94.	Solanum torvum	Solanaceae	Fruit	Doxorubicin (DOX) Induced
95.	Solanum xanthocarpum	Solanaceae	Fruits	Cisplatin
96.	Spathodea campanulata	Bignoniaceae	Bark	Gentamycin
97.	Strychnos potatorum	Loganiaceae	Seeds	Gentamycin
98.	Syzygium cumini	Myrtaceae	Fruits	Cisplatin
99.	Tamarindus indica	Fabaceae	Leaves	Cisplatin
100.	Tecoma stans	Bignoniaceae	Flowers	Gentamycin
101.	Tectona grandis	Verbanaceae	Bark	Alloxan
102.	Tephrosia purpurea (L.) Pers.	Fabaceae	Leaves	Gentamycin
103.	Thespesia populnea	Malvaceae	Leaves	Cisplatin
104.	Tinospora cardifolia	Menispermeacea	Stem	Cisplatin
105.	Trianthema portulacastrum	Aizoaceae	Leaves	Gentamycin
106.	Tribulus sativus	Zygophyllaceae	Fruits	Gentamycin
107.	Vernonia cinerea	Compositae	Aerial parts	Cisplatin
108.	Vigna munga	Fabaceae	Seeds	Rifamycin
109.	Vitex negundo linn	Verbenaceae	Bark	Chemical induced
110.	Withania somnifera	Solanaceae	Roots	Gentamycin
111.	Zingiber officinale roscoe	Zingiberaceae	Ginger Rhizome	Gentamycin

This segment is also rich in glutathione and glutathione metabolizing enzymes. The other common sites which can be affected are renal medulla, distal tubule and Loop of Henle. The renal medulla is affected mainly by polyene antibiotics and cyclosporine and that of distal tubule dysfunction is mainly due to non steroidal anti-inflammatory agents, cyclosporine, pentamidine, trimethoprim, sulphamethaxozole, amphotericin, amino glycosides, antibiotics, lithium and demeclocycline.[71]

Experimental models of nephrotoxicity:

- Acetaminophen induced nephrotoxicity
- Gentamycin induced nephrotoxicity
- Cisplatin induced nephrotoxicity
- Carbon tetrachloride induced nephrotoxicity
- Lead nitrate induced nephrotoxicity
- Cadmium induced nephrotoxicity
- Chromium-nickel induced nephrotoxicity
- Lead induced nephrotoxicity
- Hexachlorobutadiene induced nephrotoxicity
- Mercuric chloride induced nephrotoxicity
- Doxorubicin induced nephrotoxicity

Role of plants in nephroprotective function:

Many plants have been used for the treatment of kidney Failure in traditional system of medicine throughout the World. Indeed along with the dietary measures, plant Preparation formed the basis of the treatment of the disease until the introduction of allopathic medicine. Traditional Knowledge will serve as a powerful search engine and most importantly, will greatly facilitate intentional, focused and safe natural products research to rediscover the drug Discovery process.

Therefore, search of nephroprotective herbs from medicinal Plants has become important and need of the day.[11] Therefore article shows a review on some reported medicinal plants having nephroprotective activity (with their botanical Name, Family, part used and screening method).

CONCLUSION

In India, Ayurveda has provided many guidelines and remedies using plants for healthy maintenance of body in man. Nephrotoxicity has been one of the most important health issues for man. Modern medicine has no entirely effective drugs for combating nephrotoxicity without any side effects. Our traditional therapy using different parts of many plants have proved to be not only effective in treating nephrotoxicity, and without any adverse side effects. Some recent researches have proved this point to a large extent and have created a new avenue for future researchers to

make use of the existing information in developing plant based drugs in treating nephrotoxicity in this context and many other disorders in general.

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