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## Review Article

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## Effect of Nephroprotective potentials of Siddha Medicinal Herbs – A current status.

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### Abstract

Siddha system of medicine is one of the medical treatments which bring out the effective treatment for various diseases. It constitutes herbal preparation without side-effects. Among the modern world Nephro toxicity is a major problem which has threatened the human population. Thus an attempt was made in this review to reduce the nephro toxicities. In this paper the author compile the review of certain herbs with their phyto-constitutions which can protect the kidney from its toxicity.

**Keywords:** Siddha, Nephro toxicity, Nephro-protective, Herbs

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### Introduction

Siddha system of medicine is the one of the traditional medicinal system to mankind and they can prepared medicines through the siddha system more than 10000 years ago<sup>[1]</sup>.

Siddha system of medicine in practiced particularly in south Indian people. It maintains distinctive identity of own. This system closely identified with Tamil civilization. This system constitutes with no toxic effects of herbal preparations. The word Siddha comes from Siddhi that means achievements. Siddhars were the supernatural scientists with supreme knowledge<sup>[2]</sup>.

The substances which cause Nephroprotective actions must show the nephroprotective property against nephrotoxicity which is induced by Cisplatin, Gentamicin. Naturally herbs have the curative properties due to the presence of various complex chemical substances. The ancient traditional literatures has prescribed various herbs for treating renal diseases<sup>[3]</sup>.

In recent decades there is an increased rate of mortality have been seen. In order reduce the increased risk Nephro toxicity an attempt was made to compile this review. In this review author compile certain medicinal plants which protect the kidney by inducing certain Nephrotoxic substances such as Cisplatin, Gentamycin, Acetaminophen, Cadmium, Fluoride. The herbs which has the potential of protecting the kidney are as follows *Aerva lanata*, *Aegle marmelos*, *Acorus calamus*, *Anethum graveolens*, *Abutilon indicum*, *Boerhaavia diffusa*, *Cassia auriculata*, *Carica papaya*, *Curcuma longa*, *Embllica officinalis*, *Ficus religiosa*, *Lepidium sativum*, *Glycyrrhiza glabra*, *Moringa oleifera*, *Nigella sativa*, *Rubia cardifolia* Linn, *Ocimum sanctum*, *Pongamia pinnata*, *Strychnos potatorum*, *Tamarindus indica*, *Withania somnifera*.

**Nephrotoxicity agents:**

Many drugs, Chemicals and Certain diagnostic techniques are responsible for causing renal damage. Here authors have mentioned certain compounds which cause Nephrotoxicity.

Heavy metals: Mercury, lead, Arsenic and Bismuth. Antineoplastic agents :Alkylating agents: Cisplatin, cyclophosphamide. Nitrosoureas: Streptozotocin, Carmustine, Lomustine & Semustine. Antimetabolites: Methotrexate, Cytosine Arabinose, 6-thioguanine, 5-fluorouracil. Antitumor antibiotics: Mitomycin, Mithramycin, Doxorubicin. Biologic agents: Recombinant leukocyte and interferon. Antimicrobial agents: Tetracycline, Acyclovir, Pentamidine, Sulphadiazine, Trimethoprin, Rifampicin, Amphotericin B Aminoglycosides : Gentamycin, Amikacin, Kanamycin,

Streptomycin. Miscellaneous : Radiocontrast agents: Non-steroidal anti-inflammatory agents (NSAID's): Ibuprofen, Indomethacin, Aspirin etc<sup>[4]</sup>.

**Animal models used in experimental studies:****In Vivo Models:**

- GM treated albino rat
- Cisplatin treated albino rats
- Cisplatin treated rabbits
- GM treated guinea pigs
- Mercuric chloride treated mice
- Ethylene glycol treated mice

**In Vitro Models**

- Vero cells<sup>[5]</sup>

**Table No:1 Chemical constituents of some nephroprotective plants:**

S.No	Botanical name	Family	Tamil name	English name	Parts used	Chemical constituents
1.	<i>Aerva lanata</i>	Amaranthaceae	<i>Siruganpeelai</i>	Balipoovu <sup>[6]</sup>	Whole plant	Botulin, -sitosterol, Amyrin, Hentriacontane, Campesterol, Stigmasterol, Kaempferol, Starch, Propionic acid, -carboline-I, Aervoside, Aervolanine <sup>[7]</sup>
2.	<i>Aegle marmelos</i>	Rutaceae	<i>Villam</i>	Bael Holy fruit tree <sup>[6]</sup>	Leaves	Aegeline, Agelinine, Rutin, Sterol, -sitosterol, -D-glucoside, Mamesinine, Lupeol, Tannins, Phlobatannins, Flavonoids, Umbelliferone, Quercetin and Volatile oils <sup>[8]</sup> .
3.	<i>Acorus calamus</i>	Araceae	<i>Vasambu</i>	Sweet flag <sup>[6]</sup>	Aerial parts	Monoterpene, Sesquiterpene, Phenyl propanoid, Flavonoids, Quinone and basarone <sup>[9]</sup> .
4.	<i>Anethum graveolens</i>	Umbelliferae	<i>Sathakuppai</i>	The dill, Gardendill, Anet <sup>[6]</sup>	seeds	alkaloids, flavonoids, tannins, saponins, cardiac glycosides, terpenoids, anthocyanin <sup>[10]</sup>
5.	<i>Abutilon indicum</i>	Malvaceae	<i>Thuthi</i>	Indian mush mallon <sup>[6]</sup>	Whole plant	Saponins, Flavonoids and Tannins <sup>[11]</sup> .

6.	<i>Boerhaavia diffusa</i>	Nyctaginaceae	<i>Mookirattai</i>	Hog weed, Pig weed <sup>[6]</sup>	Root	Flavonoids, Alkaloids, Steroids, Triterpenoids, Lipids, Lignins, carbohydrates, Proteins and Glycoproteins <sup>[12]</sup> .
7.	<i>Cassia auriculata</i>	Fabaceae	<i>Aavaarai</i>	The tanners cassia <sup>[6]</sup>	Roots	Tannins, Di-(2-ethyl) hexyl phthalate, Alkaloids, Resins, Ca <sup>2+</sup> and Phosphorous <sup>[13]</sup> .
8.	<i>Carica papaya</i>	Caricaceae	<i>Pappaali</i>	Pappaya <sup>[6]</sup>	Seed	Flavanoids, Phenols, Alkaloids, Protein, Sterols, Terpenoids, Carbohydrates, Steroids, Tannins, Glycosides, Terpins and Saponins <sup>[14]</sup> .
9.	<i>Curcuma longa</i>	Zingiberaceae	<i>Manjal</i>	Turmeric <sup>[6]</sup>	Rhizome	Curcumin, Turmeric oil, Terpenoids, Curcumin (Terpene), Starch and Albumnoids <sup>[15]</sup> .
10.	<i>Emblica officinalis</i>	Euphorbiaceae	<i>Nelli</i>	Indian gooseberry <sup>[6]</sup>	Fruits	Vitamin-C, Carotene, Nicotinic acid, Riboflavin, D-glucose, D-fructose, Myoinositol, a Pectin with D-galacturonic acid, Darabinosyl, D-xylosyl, L-rhamnosyl, G-glycosyl, D-manosyl, D-galactosyl, Embicol, Mucic and Phyllambic acid, Phellembin, Fatty acid, Leucodelphinidine, Procyanidin, 3-O-gallated Prodelphindin, Tannins, Ellagic acid, Lupeol and Oleanolic acid <sup>[16]</sup> .
11.	<i>Ficus religiosa</i> L	Moraceae	<i>Arasu</i>	Peepul tree, Sacridfig <sup>[6]</sup>	Latex	Flavonoids, Amino acids and Tannins <sup>[17]</sup> .

12.	<i>Lepidium sativum</i>	Brassicaceae	<i>Aalivirai</i>	Garden cress, Water cress <sup>[6]</sup>	Seeds	Volatile essential Fatty oils, Carbohydrate, Protein, Vitamin B-carotene, Riboflavine, Niacin, Ascorbic acid, Flavonoids, Glycosides and Isothiocynates <sup>[18]</sup> .
13.	<i>Glycyrrhiza glabra</i>	Fabaceae	<i>Athimathuram</i>	Indian Jamaica liquorice <sup>[6]</sup>	Rhizomes	Glycyrrhizin, Glyciyrrhizic acid, Glycosides, Steroids, Glucose, Sucrose, Resin, Starch and Essential oil <sup>[19]</sup> .
14.	<i>Moringa oleifera</i>	Moringaceae	<i>Murungai</i>	Horse raddish, Drum stick <sup>[6]</sup>	Seeds	Vitamin A, Nicotinic acid, Ascorbic acid, Vitamin B, Fatty acid, Glucose, Sucrose, Citric acid, Malic acid, Succinic acid, Fumaric acid and Oxalic acid <sup>[20]</sup> .
15.	<i>Nigella sativa</i>	Ranunculaceae	<i>Karunjeeraaham</i>	Black cumin, Small fennel <sup>[6]</sup>	Whole plant	Alanine, L-Spinasterol, Arabic acid, Arginine, Amino acid, Asparagine, Aspartic acid, Carvone, Cystine, Cholesterol, Glutamic acid, Linoleic acid, Linolenic acid, Melanthin, Myristic acid, Oleic acid and Tannins <sup>[21]</sup> .
16.	<i>Rubia cardifolia</i> Linn	Rubiaceae	<i>Manjitti</i>	Indian madder <sup>[6]</sup>	Root	Purpurin, Manjistin, Garancin, Purpuroxanthin, Resin, Glucose, Sucrose, Triterpenes, Lucidine, Anthroquinine, Fattyacids and Gum <sup>[22]</sup> .
17.	<i>Ocimum sanctum</i>	Lamiaceae	<i>Thulasi</i>	Holy Basil, Sacred basil <sup>[6]</sup>	Leaves	Eugenol, Carvacrol, methyl ether, Carvacrol, Caryophyllene, Ursolic acid, Apigenin, Luteolin, Ascorbic acid, Carotene, Alkaloids, Glycosides, Saponins and Tannins <sup>[23]</sup>
18.	<i>Pongamia pinnata</i>	Papilionaceae	<i>Pungu</i>	Indian Beech <sup>[6]</sup>	Flowers	Flowers Pongamol, Protien, Alkaloids, Tannins, Sugar, Resin and Fatty oil (Karanjin) <sup>[24]</sup> .

19.	<i>Strychnos potatorum</i>	Loganiaceae	<i>Thettran</i>	Clearing nut <sup>[6]</sup>	Seeds	Flavanoids, Phenols, Saponins, Alkaloids, Steroids, Tannins, Glycosides, and Lignins <sup>[25]</sup> .
20.	<i>Tamarindus indica</i>	Caesalpinaceae	<i>Puli</i>	Tamarind <sup>[6]</sup>	Fruit pulp	Polysaccharides, Balsamine, Catechin, Nasturtium, Tamarin, Phosphatidic acid, Phosphatidic choline, Ethanollamine, Serine, Inositol, Alkaloid, Citric acid, Tartaric acid and Pottasiumbitartrate <sup>[26]</sup> .
21.	<i>Withania somnifera</i>	Solanaceae	<i>Amukkara</i>	Winter Cherry <sup>[6]</sup>	Roots	Alkaloids (Somniferon), Withaminon, Wasamin, Sugars, Glycosides, Amino acids, Essential Oils, Withaniol, Hexatriacontane, Phyto sterol and oils <sup>[27]</sup> .

### Nephroprotective plants:

#### 1. *Aerva lanata*

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Core eudicots
Order	:	Caryophyllales
Family	:	Amaranthaceae
Subfamily	:	Amaranthaceae
Genus	:	<i>Aerva</i>
Species	:	<i>lanata</i> <sup>[28]</sup>

#### Nephroprotective property:

The ethanolic extract of *Aerva lanata* shows a potent nephroprotective effect with cisplatin and gentamicin induced nephrotoxicity of either sex of white albino rats. The extract dose levels were with 75,150 and 300mg/kg shows with normal histopathology and biochemical parameters<sup>[29]</sup>.

#### 2. *Aegle marmelos*

Kingdom	:	Plantae
Clade	:	Angiosperms

Clade	:	Eudicots
Clade	:	Rosids
Order	:	Sapindales
Family	:	Rutaceae
Subfamily	:	Aurantioideae
Genus	:	<i>Aegle</i>
Species	:	<i>marmelos</i> <sup>[30]</sup>

#### Nephroprotective property:

Aqueous extract of the *Aegle marmelos* was administered with the doses of 250, 500 and 750 mg/kg to the Wistar albino rats with gentamicin induced nephrotoxicity. The aqueous extract of *Aegle marmelos* shows a potent nephroprotective effect with normal serum creatinine, urea and blood urea nitrogen level<sup>[31]</sup>.

#### 3. *Acorus calamus*

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Monocots
Order	:	Acorales
Family	:	Acoraceae
Genus	:	<i>Acorus</i>
Species	:	<i>calamus</i> <sup>[32]</sup>

***Nephroprotective property:***

The hydro alcoholic extract of *Acorus calamus* (HAE-AC, 100 and 200 mg/kg, p.o.) were given for 14 days shows the nephroprotective effect<sup>[33]</sup>

**4. *Anethum graveolens***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Asterids
Order	:	Apiales
Family	:	Apiales
Genus	:	<i>Anethum</i>
Species	:	<i>graveolens</i> <sup>[34]</sup>

***Nephroprotective property:***

The aqueous extract of *Anethum graveolens* seeds with 0.5, 1 and 2g/kg/ body wt., p.o, for 8 days, shows a nephroprotective effect against gentamicin (80 mg/kg, i.p), induced nephrotoxicity in white albino rats of either sex<sup>[35]</sup>.

**5. *Abutilon indicum***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Malvales
Family	:	Malvaceae
Genus	:	<i>Abutilon</i>
Species	:	<i>indicum</i> <sup>[36]</sup>

***Nephroprotective property:***

The Ethanolic extract of *Abutilon indicum* possess a scavenging superoxide and hydroxyl radicals and results reduction of lipid peroxidation in cisplatin induced nephrotoxicity shows a nephroprotective effect on histopathological and biochemical screening<sup>[37]</sup>.

**6. *Boerhaavia diffusa***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Order	:	Caryophyllales
Family	:	Nyctaginaceae
Genus	:	<i>Boerhavia</i>
Species	:	<i>diffusa</i> <sup>[38]</sup>

***Nephroprotective property:***

On observing the clinical, experimental and immunological studies of *Boerhaavia diffusa* shows diuretic effect which is equivalent to furosemide. It increases serum protein level and decreases the excretion of protein in nephrotic syndrome. Thus clinically it has been proved as a safer drug for nephrotic syndrome<sup>[39]</sup>.

**7. *Cassia auriculata***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Fabales
Family	:	Fabaceae
Genus	:	<i>Cassia</i>
Species	:	<i>auriculata</i> <sup>[40]</sup>

***Nephroprotective property:***

The alcoholic root extract of *Cassia auriculata* shows a potent nephroprotective effect against cisplatin and gentamicin induced nephrotoxicity with normal blood urea and Creatinine levels and also the biochemical studies<sup>[41]</sup>.

**8. *Carica papaya***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Brassicales
Family	:	Caricaceae
Genus	:	<i>Carica</i>
Species	:	<i>papaya</i> <sup>[42]</sup>

***Nephroprotective property:***

An Ethanolic extract of *Carica papaya* shows *Nephroprotective property of cisplatin* (10mg/kg, i.p.) induced nephro toxicity was proven through gross behavioral studies, histopathological, renal function and biochemical studies. It also have scavenging activity, lipid peroxidation of kidney. Thus it shows nephroprotective in nature<sup>[43]</sup>.

**9. *Curcuma longa***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Monocots
Order	:	Zingiberales
Family	:	Zingiberaceae
Genus	:	<i>Curcuma</i>
Species	:	<i>longa</i> <sup>[44]</sup>

***Nephroprotective property:***

On treating with Curcumin in the doses of 100, 200, and 400 mg/kg for 10 days in rats. It shows a potent nephroprotective effect on the histopathological and biochemical screening<sup>[45]</sup>.

**10. *Emblica officinalis***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Malpighiales
Family	:	Malpighiales
Genus	:	<i>Phyllanthus</i>
Species	:	<i>emblica</i> <sup>[46]</sup>

***Nephroprotective property:***

The extract of *Emblica officinalis* shows a potent nephroprotective effect with gentamicin (150mg/kg/day) induced in female rats<sup>[47]</sup>.

**11. *Ficus religiosa L***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Rosales
Family	:	Moraceae
Genus	:	<i>Ficus</i>
Species	:	<i>religiosa</i> <sup>[48]</sup>

***Nephroprotective property:***

The methanolic extract of *Ficus religiosa* shows a potent nephroprotective effect and curative effect with cisplatin (5mg/kg, i.p.) induced nephrotoxicity with normal biochemical levels<sup>[49]</sup>.

**12. *Lepidium sativum***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Brassicales
Family	:	Brassicaceae
Genus	:	<i>Lepidium</i>
Species	:	<i>sativum</i> <sup>[50]</sup>

***Nephroprotective property:***

The ethanolic extract of *Lepidium sativum* with 400mg/kg shows a nephroprotective effect against cisplatin (5mg/kg, i.p.) induced nephrotoxicity<sup>[51]</sup>.

**13. *Glycyrrhiza glabra***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Fabales
Family	:	Fabaceae
Genus	:	<i>Glycyrrhiza</i>
Species	:	<i>glabra</i> <sup>[52]</sup>

***Nephroprotective property:***

The extract of *Glycyrrhiza glabra* shows a potent nephroprotective effect with gentamicin (150mg/kg/day) induced in female rats<sup>[53]</sup>.

**14. *Moringa oleifera***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Brassicales
Family	:	Moringaceae
Genus	:	<i>Moringa</i>
Species	:	<i>oleifera</i> <sup>[54]</sup>

***Nephroprotective property:***

The aqueous ethanolic extract of *Moringa oleifera* leaves (150 and 300 mg/kg) shows the potent nephroprotective action against gentamicin induced nephrotoxicity<sup>[55]</sup>.

**15. *Nigella sativa***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Ranunculales
Family	:	Ranunculaceae
Genus	:	<i>Nigella</i>
Species	:	<i>sativa</i> <sup>[56]</sup>

***Nephroprotective property:***

*Nigella sativa* oil (0.5, 1.0 or 2.0 ml/kg/day) was orally administered in rats with gentamicin (80 mg/kg/day i.m) induced nephrotoxicity. Thus the histopathological and biochemical values shows that the oil of *Nigella sativa* have nephroprotective effect<sup>[57]</sup>.

**16. *Rubia cordifolia* Linn**

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Asterids
Order	:	Gentianales
Family	:	Rubiaceae
Genus	:	<i>Rubia</i>
Species	:	<i>cordifolia</i> <sup>[58]</sup>

***Nephroprotective property:***

The hydroalcoholic extract of *Rubia cordifolia* root possess the effect of nephroprotection against ethylene glycol induced urolithiasis which was proved by histopathological and biochemical screening<sup>[59]</sup>.

**17. *Ocimum sanctum***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Asterids
Order	:	Lamiales
Family	:	Lamiaceae
Genus	:	<i>Ocimum</i>
Species	:	<i>sanctum</i> <sup>[60]</sup>

***Nephroprotective property:***

The seeds of *Ocimum sanctum* is useful in the treatment of urinary disorders<sup>[61]</sup>.

**18. *Pongamia pinnata***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Fabales
Family	:	Fabaceae
Genus	:	<i>Pongamia</i>
Species	:	<i>pinnata</i> <sup>[62]</sup>

***Nephroprotective property:***

The ethanolic extract of *Pongamia pinnata* flowers (300 & 600mg/kg) was orally administered in rats with cisplatin (5mg/kg ip) induced nephrotoxicity shows a potent nephroprotective effect with normal histopathological and biochemical screening<sup>[63]</sup>.

**19. *Strychnos potatorum***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Asterids
Order	:	Gentianales
Family	:	Loganiaceae
Genus	:	<i>Strychnos</i>
Species	:	<i>potatorum</i> <sup>[64]</sup>

***Nephroprotective property:***

The Ethanolic extract of seeds of *Strychnos potatorum* shows nephroprotective effect against gentamicin induced nephrotoxicity<sup>[65]</sup>.

**20. *Tamarindus indica***

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Fabales
Family	:	Fabaceae
Genus	:	<i>Tamarindus</i>
Species	:	<i>indica</i> <sup>[66]</sup>

***Nephroprotective property:***

The 70% aqueous ethanolic extract of *Tamarindus indica* with a dose of 200mg/kg were given for three weeks with gentamicin 80mg/kg against nephrotoxicity in male rabbit. The histopathological



and biochemical screening shows the potent nephroprotective effect<sup>[67]</sup>.

### 21. *Withania somnifera*

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Asterids
Order	:	Solanales
Family	:	Solanaceae
Genus	:	<i>Withania</i>
Species	:	<i>somnifera</i> <sup>[68]</sup>

#### ***Nephroprotective property:***

Cadmium induced nephro toxicity was prevented by *Withania somnifera*. Mice were given with cadmium chloride with Aswagandha extract and Aswagandha extract alone which was given (1.14g/kg body weight) for 20 days. lipid peroxidation shows that Aswagandha has a ability of reducing nephro toxicity<sup>[69]</sup>.

### Conclusion

In this review the authors provide certain numbers of medicinal plants with its chemical constitutes which helps to protect the kidney from nephrotoxic agents. This review will provide footsteps for clinically in nephrotoxicity patients.

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