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CRITICAL REVIEW AND ANALYSIS OF NEPHRO-PROTECTIVE DRUGS IN AYURVEDA

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ABSTRACT

Medicinal plants may serve as a vital source of potentially useful new compounds for the development of effective therapy to combat a varieties of Kidney problems. Many herbs have been proven to be effectual as Nephro-protective agents. Developing a satisfactory herbal therapy to treat severe renal disorders, requires systematic investigation of properties like Acute Renal Failure (ARF), Nephrotic syndrome and chronic interstitial nephritis. Chronic Renal Failure (CRF) is considered when glomerular filtration rate (GFR) falls below 30ml/min.The conventional approach of management includes Dialysis and Renal Replacement Therapy (RRT) which are not affordable by Indian Populations due to economic status. Therefore, exploration of a safe and alternative therapy is needed. In Ayurveda, some of the herbs possess Nephro-protective properties due to presence of their chemical components likeKanchnar(*Bauhinia variegata*)), Kushmanda (*Benincasa hispida*),Yeshtimadhu (*Glycyrrhiza glabra*). The present review is aimed to elucidate the list of Nephro-protective medicinal plants, which are scientifically proved in treating renal disorders.

Keywords-

Kidney disease, Ayurveda, Nephro-protective

Introduction-

Nephrotoxicity is one of the most commonly kidney problems and occurs when body is exposed to a drug toxicity [1]. A number of therapeutic agents can adversely affect the kidney, resulting in Acute Renal Failure (ARF), Chronic interstitial nephritis and nephrotic syndrome. There is an increasing number of potent therapeutic drugs like aminoglycosides antibiotics, Non-steroidal anti-inflammatory drugs, Chemotherapeutic agents have been added to the therapeutic arsenal in recent years [2]. Exposure to chemical reagents like ethylene glycol, carbon tetra chloride, sodium oxalate and heavy metals such as lead, mercury, cadmium, arsenic includes nephrotoxicity. Prompt recognition of the disease and cessation of responsible drugs are usually the only necessary therapy [3]. Nephroprotective agents are the drugs which possess protective activity against nephrotoxicity. Medicinal plants have curative properties due to presence of various complex chemical substance. Early literatures have prescribed various herbs for the cure of renal disorders [4]. The term renal failure primarily denotes failure of the excretory function of kidneys, leading to retention of nitrogenous waste products of metabolism in the blood [5]. In addition to this, there is a failure of regulation of fluid and electrolyte balance along with endocrine dysfunction. The renal failure is fundamentally categorized into acute and chronic renal failure [6].

Acute Renal Failure (ARF) refers to the sudden and usually reversible loss of renal function, which develops over a period of days or weeks. There are many causes for Acute Renal Failure (ARF) which mainly includes Acute Tubular Necrosis (ATN) that commonly occurs for 85% of incidence. Mostly acute tubular necrosis occurs either due to exogenous or endogenous. The exogenous agents are radio-contrast

agents, cyclosporine, antibiotics, chemotherapeutic agents [5,6]. Chronic Renal Failure (CRF) is an irreversible deterioration in the renal function which classically develops over a period of years, leading to loss of excretory metabolic and endocrine functions, various causes of renal failure has been recognized like Hypertension, Diabetes mellitus, Antineoplastic agents like cyclophosphamide, vincristine, cisplatin etc. [5]

In Ayurveda, Chronic Kidney Disease (CKD) described as a mooltra dosha vikara and causing an edema. Both kidney are root of medovahasrotas [7]. According to Acharya Charaka the causes of mooltra dosha vikara are vitiated by the intake of unhealthy drinks and foods, sexual intercourse while having the urge of micturition, disorder of electrolyte imbalance, malnutrition, and severe traumatic injury [7].

Pathogenesis Of Kidney Disease In Ayurveda

The pathogenesis of kidney diseases is not separately mentioned. It can be included in Prameha, Mooltra dosha, Mootrakriccha, injury of vankshana, Ashmari and Shotha etc. In Charaka Samhita, described that kidney and bladder are the root (controlling organ) of the channels carrying urine and fat, mamsa and liquid dhatus of the body. The vitiated doshas while coming in contact with the opening of these channels obstruct them. This result in the manifestation of kidney disease. While become chronic or incurable due to the affection of all the qualities of doshas and also due to the simultaneous vitiation of dhatus [8].

Agents which Causes Nephrotoxicity

Drugs, diagnostic agents and chemicals (fertilizers, pesticides) are well known to be nephrotoxic. The following are some of the important nephrotoxic agents [9].

- A) Heavy metal-
Mercury, Arsenic, Lead
- B) Anti-neoplastic agents
 - a) Ankylating-agents-Cisplatin, cyclophosphamide
 - b) Nitrosoureas-Carmustine
 - c) Anti-Tumour Antibiotics- Doxorubicin
- C) Anti-microbial-
Tetracycline, Acyclovir, Trimethoprim, Rifampicin, Amphotericin-B
- D) Aminoglycosides-
Gentamycin, Amikacin, Kanamycin, Streptomycin
- E) Misc.
 - a) Radio-contrast-agents- NSAID's, Ibuprofen, Indomethacin, Aspirin

Concept Of Nephro-protective Drugs in Ayurveda

In Ayurveda text, some herbs are mentioned having specific actions on Mutravahasrotas (Urinary System) and its diseases. These herbs are classified under Mutravirechaneeya Gana are Diuretic in action and Mutraviranjaneeya Gana acts on removal of dushita doshas from urine [7].

Materials and Methods-

Materials -

Data are collected from various classical *Samhita* of Ayurveda and their commentaries, modern medicine books, published research articles, paper, journals and internet.

Methods -

Type of study: - Critico-conceptual study

Plants with Nephroprotective effects-

The following plants are having Nephro-protective activity

***Bauhinia variegata* (Kanchnar)**

Nephroprotective activity of the ethanolic and aqueous extracts of root of

Bauhinia variegata at a dose of 400 mg/kg bw was evaluated by gentamicin and cisplatin induced nephrotoxicity in rats. Both extracts showed nephroprotective activity in both gentamicin and cisplatin induced nephrotoxicity models as evident by decrease in serum creatinine, serum urea, urine creatinine and BUN levels in extract treated groups which was elevated by gentamicin and cisplatin in the respective models, which also confirmed by histopathological study [10-11].

***Benincasa hispida* (Kushmanda)**

Hydro-alcoholic extract of *Benincasa hispida* whole fruit extract significantly increased the tissue GSH levels and reduced lipid peroxidation levels. Furthermore, it was confirmed by the histopathological observation that the degenerative changes caused by paracetamol were also restored by treatment with hydro-alcoholic extract of *Benincasa hispida* whole fruit extract [7-8]. It was also produced nephroprotective activity against mercury poisoning in rats [12-13].

***Tribulus terrestris* (Gokshura)**

Diuretics-Rich in potassium and nitrates [14]

***Brassica nigra* (Rajkshavak)**

The crude methanol extract of *Brassica nigra* leaf lacks inherent toxicity and exhibits hepatic and nephroprotective [15-16].

Brassica rapa

The effect of the ethanol extract of the roots of *Brassica rapa* (EBR) to ameliorate cisplatin-induced nephrotoxicity was studied in terms of oxidative stress, as characterized by lipid peroxidation, reactive oxygen species (ROS) production, and glutathione (GSH) depletion in LLC-PK1 cells [17].

Bryophyllum calycinum

The aqueous extract of the leaves possessed potent nephroprotective

activity in gentamycin-induced nephrotoxicity in rats. The plant hydroalcoholic extract was also found to exert significant diuresis and antiurolithitic activity when given by oral and ip route to rats [18-21].

***Carum carvi* (Krishna Jeeraka)**

The renoprotective effect of aqueous extract of *Carum carvi* seeds was evaluated in experimentally induced diabetic nephropathy (DN) in rodents. The morphological examination of untreated diabetic rats kidneys showed glomerular and tubular degeneration with massive cellular infiltration, hemorrhage in interstitial tissue and deformed renal tissue architecture. Whereas the kidney of *Carum carvi* essential oil treated rats showed marked improvement with minor pathological changes [22-23].

***Cassia occidentalis* (Kasmarda)**

The nephroprotective activity of the 70% hydroalcoholic extract of *Cassia occidentalis* was tested against gentamicin induced nephrotoxicity in rats.[24-26]

Casuarina equisetifolia

The nephroprotective activity of methanolic extract of *Casuarina equisetifolia* leaves was studied in gentamicin induced nephrotoxicity in Wistar rats. *Casuarina equisetifolia* leaves extract ameliorates gentamicin-induced nephrotoxicity and oxidative damage by scavenging oxygen free radicals, decreasing lipid peroxidation and improving intracellular antioxidant defense [27-28].

Citrullus colocynthis

The nephropathy protective effect of *Citrullus colocynthis* fruits extract was studied in streptozotocin induced diabetes in rats. The study clearly demonstrated that *Citrullus colocynthis* fruit exerted protective effects on the kidney functions and tissues. So it

may play a role in prevent nephropathy as one of microvascular complications of diabetes mellitus [25-26].

***Crocus sativus* (Kumkum)**

The protective effects of saffron extract and crocin was evaluated in chronic - stress induced oxidative stress damage of the brain, liver and kidneys in rats. Chronic stress, the levels of the lipid peroxidation product, malondialdehyde (MDA), the total antioxidant reactivity (TAR), as well as antioxidant enzyme activities glutathione peroxidase (GPx), glutathione reductase (GR) and superoxide dismutase (SOD) were measured in the brain, liver and kidneys tissues after the end of chronic stress[29-30]

***Cuminum cyminum* (Jeeraka)**

The effect of *Cuminum cyminum* (Cumin) on kidney exposed to profenofos was evaluated in female swiss albino mice. The results showed that cumin was effective in normalizing the uric acid and creatinine level [31-32].

Cymbopogon schoenanthus

Cymbopogon schoenanthus extract has prophylactic effect in oxalate stone formation [35-36].

***Cynodondactylon* (Durva)**

Cynodondactylon extract reduced the levels of calcium oxalate deposition especially in medullary and papillary sections from of the kidney of the treated rats [35].

***Daucus carota* (Garjar)**

The renoprotective activity of *Daucus carota* root extract was studied in renal ischemia reperfusion injury in rats. *Daucus carota* extracts was associated with a significantly lower malondialdehyde level. Accordingly, *Daucus carota* extracts exerted renoprotective activity probably by the free radical scavenging activity [36-37].

Foeniculum vulgare (Mishreya)

The aqueous extract of *Foeniculum vulgare* seeds, *Solanum nigrum* fruit and their mixture significantly prevented renal damage by normalizing increased levels of renal markers. Mixture of both plants at high doses exhibited improved nephroprotective and antioxidant activities [38].

Glycyrrhiza glabra (Yeshtimadhu)

Polyuria in rats with gentamicin-induced acute renal failure was associated with down-regulation of renal aquaporin 2 in the inner and outer renal medulla, and

cortex. Glycyrrhizin (200 mg/kg/day) administration restored the expression of aquaporin 2 with paralleled changes in urine output. The changes in renal functional parameters (creatinine clearance, urinary osmolality, and solute-free reabsorption), accompanying acute renal failure were also partially restored after administration of glycyrrhizin. Histological changes in rats with gentamicin-induced acute renal failure were also abrogated by glycyrrhizin treatment [39].

Table 2: Research Work Done On Nephro-protective Drugs[41]

Sr No	Botanical name	Family	Part used	Chemical constituents	Screening method	References
1	<i>Aerva lanata</i> (<i>Gorakshganja</i>)	Rutaceae	Whole plant	Botulin, β -sitosterol, Amyrin, Hentriacontane, Campesterol, Stigmasterol, Kaempferol, Propionic acid, β -carboline-I, Aervoside and Aervolanine	Gentamicin induced	Paller et.al., 19904
2	<i>Crataevanurvula</i> (<i>Varuna</i>)	Cappariaceae	Fruit	Kaemferol-3-O-a-D-glucoside, Quercitin-3-O-a-D-glucoside, Flavanoids, Glucosinolates, Steroids, Lupeol and Tannins	Gentamicin induced	Kore et.al., 20114
3	<i>Orthosiphon stamineus</i> (<i>Java tea</i>)	Laminaceae	Whole plant	Flavanoids, Phenols, Carbohydrates, Steroids, Tannins, Glycosides, Terpins and Saponins	Gentamicin induced	Kannapan et.al.,201041
4	<i>Strychnospotatorum</i>	Loganiaceae	Seed	Flavanoids, Phenols, Saponins, Alkaloids, Steroids, Tannins, Glycosides, and Lignins	Gentamicin induced	Ruby Varghese et.al., 201142
5	<i>Aerva javanica</i>	Amaranthaceae	Fresh roots	Isoquercetin, 5 methylmellein, 2-hydroxy-3-O- β -	Cisplatin induced	Vinit movaliya et.al.,

				primeveroside naphthalene-1,4- dione, Apigenin7- Oglucoronide and Kaempferol		201143
6	<i>Carica papaya</i> (Papita)	Caricaceae	Seed	Flavanoids, Phenols, Alkaloids, Protein, Sterols, Terpenoids, Carbohydrates, Steroids, Tannins, Glycosides, Terpins and Saponins	Cisplatin induced	Subal debnath et.al., 201044
7	<i>Ficus religiosa</i> L (Vata)	Moraceae	Latex	Flavonoids, Amino acids and Tannins	Cisplatin induced	Yogesh chandyadav et.al., 2011
8	<i>Pedaliium murex</i> Linn (BrihataGokshu ra)	Pedaliaceae	Dried fruits	Flavanoids, Flavones, Alkaloids, Triterpenoids, Carbohydrates, Glycosides and Saponins.	Cisplatin induced	Shelke et.al., 200946
9	<i>Vernonia</i> <i>cinerea</i> (Sahadevi)	Compositae	Aerial parts	Triterpenoids like α -amyrin, β -amyrin and lupeol	Cisplatin induced	Sreedevi et.al., 201147
10	<i>Acorus calamus</i> (Vacha)	Araceae	Aerial parts	Monoterpene, Sesquiterpene, Phenyl propanoid, Flavonoids, Quinone and basarone	Acetamino phen induced	Palani et.al., 201048
11	<i>Boerhaaviadiffusa</i> (Punernava)	Nyctaginaceae	Root	Flavonoids, Alkaloids, Steroids, Triterpenoids, Lipids, Lignins, carbohydrates, Proteins and Glycoproteins	Acetamino phen induced	Surendra et.al., 201149
12	<i>Indigofera</i> <i>barberi</i> L (Neela)	Fabaceae	Whole plant	Flavonoids, Phenolic acid and sterols	Acetamino phen induced	Palani et.al., 200850
13	<i>Pimpinella</i> <i>tirupatiensis</i>	Apiaceae	Whole plant	Alkaloids, Flavonoids, Flavones, Volatile oils, β - Bisabolone, Δ -3- Carene, Cis-Carveol, Enemol, Δ -Carveol	Acetamino phen induced	Palani et.al., 200951

				and Methylgeranate		
14	<i>Curcuma longa</i> (<i>Haridra</i>)	Zingiberaceae	Rhizome	Curcumin, Turmeric oil, Terpenoids, Curcumin (Terpene), Starch and Albumnoids	Cadmium induced	Eduardo Molina-Jijon et.al., 2011
15	<i>Drynaria fortune</i>	Polypodiaceae	Whole plant	Arsenic, Ca ²⁺ , Cu ²⁺ , Glucose, Iron, Mg, Mn, Hg, Naringin, K ⁺ , Na ⁺ , Starch and Zinc	Silver chloride induced	Kore et.al., 201153
16	<i>Eruca sativa</i> (<i>Tuvari</i>)	Crassulaceae	Seeds	Flavanoids	Mercuric chloride induced	Sarwar Alam et.al., 200754
17	<i>Moringa oleifera</i> (<i>Shigru</i>)	Moringaceae	Seeds	Vitamin A, Nicotinic acid, Ascorbic acid, Vitamin B, Fatty acid, Glucose, Sucrose, Citric acid, Malic acid, Succinic acid, Fumaric acid and Oxalic acid	Fluoride induced	Ranjan et.al., 200955
18	<i>Tamarindus indica</i> (<i>Chincha</i>)	Caesalpiniaceae	Fruit pulp	Polysaccharides, Balsamine, Catechin, Nasturtium, Tamarin, Phosphatidic acid, Phosphatidic choline, Ethanollamine, Serine, Inositol, Alkaloid, Citric acid, Tartaric acid and Pottasiumbitartrate	Fluoride induced	Ranjan et.al., 200955
19	<i>Tectona grandis</i> (<i>Shaka</i>)	Verbanaceae	Bark	Lapachol, Dehydro- α -lapachone, Methyl quinizarin and Squalene.	Alloxan induced	Ghasias et. al., 201056
20	<i>Ginkgo biloba</i>	Ginkgoaceae	Whole plant	Flavonoids, Bilobalide, Ginkgolide A, Ginkgolide B and Ginkgolide C and Biflanoide	Streptozotocin induced	Welta et.al., 200757
21	<i>Abutilon</i>	Malvaceae	Whole	Saponins,	Gentamicin	Kakasaheb

	<i>indicum</i> (<i>Atiibala</i>)	ae	plant	Flavonoids Tannins.	and	induced	Khore et.al., 201158
22	<i>Euphorbia</i> <i>neriifolia</i> (<i>Snuhi</i>)	Euphorb iaceae	Leaves	Saponins, Flavonoids Tannins	and	N-nitroso dimethyl amine induced	Pracheta et.al., 201159
23	<i>Rubia cardifolia</i> Linn (<i>Manjishtha</i>)	Rubiace ae	Root	Purpurin, Manjistin, Garancin, Purpuroxanthin, Resin, Glucose, Sucrose, Triterpenes, Lucidine, Anthroquinine, Fattyacids Gum.	and	Ethylene glycol induced	Kalyani Divakar et. al., 201060
2 4	<i>Punicagranatu</i> <i>m L</i> (<i>Dadima</i>)	Puniace ae	Fruit peel	Ellagic acid, Ellagitannins gallic acid.	and	Ferric nitri lo tri acetate induced	Mahgoub Mohammed AHMED et.al., 201061

Observation and Discussion-

The alcoholic and aqueous extracts of the *Hybanthus enneaspermus* possesses significant curative and preventive nephroprotective activity. According to Acharya charak, mootra dosh vikara is tretised by punarnava, haritaki, shunthi, nagarmotha, shilajeet, Gokshura, yavakshar etc. Kansharitaki is also very helpful in mootra dosha vikar as well as vata-kaph odema. Shilajeet is helpful with take gomutra in mootra dosha vikar. *Tectona grandis* has the potential to treat diabetes mellitus and prevent the associated renal damage. Traditionally *Tectona grandis* is used in treatment of diabetes, lipid disorders, inflammation, ulcer, and bronchitis. *Tectona grandis* is reported to have antiulcer, antimicrobial, wound healing, anticancer, and anti-renal damage activity. Chronic kidney disease (CKD) can be prevented or delayed by early

treatment using angiotensin II-converting enzyme inhibitors and angiotensin II-receptor blockers. A great amount of the world's population has been using traditional Chinese herbal medicine (astragalus; angelica; rhubarb) for treatment of CKD. Listed selected plants as like in table used by Aboriginal tribes all over Canada for kidney diseases. Mostly, these are used for diuresis, renal stones and cleansing the kidneys. A brief review of the literature shows different plants being effective in preventing/treating renal diseases. Some renal conditions reported to respond to plant therapy are glomerulonephritis, IgA nephropathy, membranous nephropathy, glomerulosclerosis, immune complex nephritis, nephrotic syndrome, lupus, tubule interstitial nephritis, chronic allograft nephropathy, kidney stones etc. Some pharmacological

characteristics seen in plants that may contribute in the abovementioned conditions are anti-inflammation; antioxidation. The therapeutic property of *Sesamum indicum* seeds propitious in improving nephropathy by significantly improving serum parameters and histopathological evidence also suggests the same. The seed contains appreciable amounts of various bioactive components including tocopherols, phytosterols, resveratrol and flavonoids, and the lignans sesamin and sesamolin. The identification and management of early stage diabetic kidney disease is important, but the majority of people exhibit no symptoms until the disease is more advanced renal damage. Hemidesmus indicus was found on study base that aqueous and methanolic extracts have more significant inhibitory effect on salt water feeding induced severity of microalbuminuria, serum urea and creatinine, myocyte diameter and retention of Na⁺ and water and increases the serum calcium level. It is potent natural nephroprotective also a cardioprotective. *Orthosiphon stamineus* is the one of the important medicinal plant which used for kidney based Problems traditionally. The ethanolic extracts of *O. stamineus* leaves have been used for the nephroprotective activity. The whole plant of the *Orthosiphon stamineus* (cats whiskers) is used as gall bladder, kidney, liver, bladder problems, painful tooth, hypertension and genitourinary diseases. Cat's Whiskers is a perennial herb found mainly throughout south East Asia and tropical Australia. The herb is popularly known as Java tea. *O. stamineus* is used widely in the form of herbal tea among the South East Asian population.

Pharmacological properties of Polyphenols are found in the renal area, acting as diuretic, anti-inflammatory, antispasmodic, and antioxidant agents. Various polyphenolic compounds have been reported for their nephroprotective activity with a good level of renal protection. Therefore, considering the important role of polyphenolic compounds in the prevention or reduction of renal disorders induced by various nephrotoxic chemical agents, in this way, he was summarized the some antioxidant plants, such as, *Achyrocline satureioides*, *Zingiber officinalis*, *Teminalia chebulata* etc having Nephroprotective properties. *Solanum nigrum* was found that renal markers (urea, serum creatinine, uric acid) were brought back to normal. Thus it is inferred that *Solanum nigrum* preserves the functional capacity of the kidney against ethanol toxicity. *Launaea procumbens* effectively protect kidneys as well as decreased Serum level of creatinine, urobilinogen, BUN, direct bilirubin, total bilirubin and globulin while total proteins, albumin, through antioxidant and free radical scavenging effects of flavonoids and saponins.

Conclusion-

From this study, it is clear that the medicinal plants play a prominent role against various diseases. A variety of medicinal plants and plants extracts have been reported for its significant nephroprotective activity in animal models. The nephroprotective activity is probably due to the presence of Flavanoids in all the few medicinal plants. The results of this study indicate that extracts of leaves and plants of some

medicinal plants have good potentials for use in kidney damages.

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