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Aspect of Herbal Drug, Avoidance and Management of Kidney Disease

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ABSTRACT

Renal function disorders have always underestimated since ages. It is one of the foremost reasons of demise in the world. Alarming incidence of kidney failure is increasing day by day. The usage of herbal drugs for the avoidance and management of kidney disorders are persistently developing all over the world. A large number of extracts of natural goods and nutritional antioxidants have been noted to display protective effects against nephrotoxicity. Many *Ayurvedic* herbal drugs have revealed a very good effect as Nephroprotective drugs due to their antioxidant, anti-inflammatory, diuretic and antispasmodic properties. WHO has recently mentioned that traditional medicines have been existing in therapeutic practice even hundred years before the development of scratch of modern medicine. There is mounting an awareness of herbal health benefits. This is with good reason as they might offer a natural protection against the development of conditions and be a treatment for some diseases. Herbal drugs have clinically confirmed great immunomodulation, adaptogenic and anti-mutagenic, they play a very important role in the treatment of urinary stones. A series of medicinal plants shows Antiurolithiatic activity such as *Shigru, Pashanabheda, Sariva, Punarnava, Gokhuru, Makka,Varun & Methika* as they reduce elevated blood urea & Serum Creatinine. *Sariva* & *Shigru* increases the functional capacity like prevention of renal injuries; helps in improving Haemopoiesis, Such many valid evidences are required to provide scientific evaluation for the use of traditional medicines in the development of preventive and personalized medicine.

KEYWORDS

Kidney disease, Herbal drug, Ayurveda, Prevention and management

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INTRODUCTION

The prevalence of renal diseases is increasing globally. Common kidney problems include- Urinary tract infection (UTI), Glomerulonephritis, Nephritic syndrome, renal failure etc. Nephrotoxicity is very common kidney disease, often elicited when body is exposed to a medicine or toxin. With the advancement of kidney damage, the body is unable to discard excess wastes from the body. Blood electrolytes just like Potassium and Magnesium are sharply elevated. A series of therapeutic functionary can skeptically affect the kidney culminating in nephritic syndrome, chronic intestinal nephritis and acute renal failure because augmenting statistics of potent therapeutic drugs like chemotherapeutic agents, antibiotics, aminoglycoside and NSAIDs have been added to the therapeutic armory in recent times. Susceptibility to chemical reagents like carbon tetrachloride, ethylene glycol, sodium oxalate and heavy metals like lead (Pb), mercury (Hg), arsenic (As) and cadmium (Cd) also leads to nephrotoxicity. *Ayurvedic* herbs have played a significant role in various ancient traditional systems of medicine. Even now-a-days, plants serve as a cheap source of drugs for greater mass of world's population. Pharmacological progress on the medicinal plants used in traditional lithotripter, antiurolithic treatments has shown their therapeutic prospect in the in-vitro or in-vivo models[1]. Plentiful of plants have been used for the analysis of kidney failure in Ayurveda. Certainly along with the dietary measures, plant preparation formed the basis of the treatment of the disease until the exordium of modern allopathic medicine.

Various herbal drugs have contrasting mechanism to treat Urolithiasis.

1) Physiological pH alteration: Urine pH is the leading aspect that predominantly identifies the type of urine calculus i.e., Crystalluria is pH dependent[2]. Different precipitation may specify as follows:

At urine pH $\leq$5.0 - the pure uric acid,

pH from 5.2 to 5.8- the salts of uric acid,

pH from 5.0 to 6.0- oxalates and pH= 7 hydroxyapatite are precipitated. Solubilisation of these calculi can be attained by alteration of urinary pH. An increase in urinary pH might be responsible subject for dissolving complex of calcium & oxalate crystals[3].

2) Antioxidant property: Affliction to the epithelial cells of the kidney in the companionship of calcium is mediated by the overproduction of reactive oxygen species (ROS), formed mostly from mitochondria or nicotinamide adenine di-nucleotide phosphate (NADPH) oxidase. The interaction between damaged renal

tubular epithelium and Calcium oxalate ions are likely to play a serious role in the development of urinary stones[4]. Some ayurvedic herbal drugs like *Curcuma longa (Haridra), Hordeum vulgare (Barley), Zingiber officinale (Shunthi), Punica granatum (Dadima)* have anti-oxidants properties.

3) Diuretic activity: Increasing urine output volume shrinks the saturation of salts & prevents precipitation of crystal at physiological pH. Almost every herbal medicine used for treatment of urolithiasis has some diuretic action and alkalizer property[5].

4) Suppression of oxalate synthesizing enzyme: *Tribulus terrestris (Gokshura)*- The antiurolithic activity is attributed to its GOX inhibition[6]. *Crataeva nurvala (Varuna)* - reduced oxalate synthesizing enzyme (lactate dehydrogenase & Glycolic acid oxidase), diminished marker of crystal deposition in the kidney and confirmed that it can be used as curative agent in urolithiasis[7]. Kaempherol & Quercetin, the active components, were found to be competitive inhibitors of GOX and non-competitive, respectively[8].

5) Mixed action: Corn silk diminishes irritation, increases urine output secretion & in addition, it holds excellent antioxidant capacity. It was reported that the alcoholic extract of anti-urolithiatic activity in dissolution of regenerated Calcium oxalate crystals[9].

Ayurveda has many medicinal plants useful in the management of Renal diseases are as follows:-

Guduchi:- *Tinospora cordifolia* (Menispermaceae)- *Guduchi* have diuretic effect, antidepressant, memory improving, antioxidant effect. Studies have shown antibacterial action of extracts of leaves and stem of *Guduchi* which were experienced on clinical isolates of urinary pathogens such as *Klebsiella pneumoniae*, *Escherichia coli* and *Pseudomonas aeruginosa*. The ethanolic extract of *Guduchi* stem have inhibitory action on calcium oxalate crystals thus may be beneficial in the management of urolithiasis. Diuretic action may also diminish the calculi growth after increasing total fluid intake and such effects have been attributed to several herbal formulations[10].

Methika:- *Trigonella foenum-graecum* (Fabaceae)- Fenugreek seeds have been used traditionally by many of *Ayurvedic* doctors for kidney ailments. *Methika* is the dominant alkaloid. It acts by suppression of oxidative stress in kidney and decrease in renal cell apoptosis and fibrosis. This drug shows diuresis, antioxidant action and let down urinary concentrations of calculi making constituents as a very good for anti-urolithiatic action[11].

***Kulattha*:-** *Dolichos biflorus* have reduced the recurrence of Calcium oxalate stone and it is having a superior effect than conventional potassium citrate[12].

***Punarnava*:-** *Boerhaavia diffusa* Linn (*Nyctaginaceae*). It is extensively used in Ayurvedic system of medicine for different renal disorders including Calcium oxalate urolithiasis. Studies have revealed that, its antioxidant activity protects kidney from hyper-oxaluric oxidative stress and renal cell injury[13]. It is verified to be nephro-protective agent.

***Varuna*:-** *Crataeva nurvala* Buch. Ham. (*Capparidaceae*) in *Sushruta Samhita Varuna* is described in most of urinary disorders including urolithiasis[14].

Stem bark of *Varuna* comprises lupeol. Lupeol has cytoprotective effect on free radical toxicity which is investigated in experimental study on urolithiasis[15]. Decrease in kidney oxalate levels was seen after administration of lupeol, which is also effective in countering the free radical toxicity by bringing about decrease in peroxidative levels and an increase in antioxidant status[16].

***Ashwagandha*:-** *Withania somnifera (Solanaceae)* root is known to have nephroprotective effect. In an experimental study it was understood that, urea, creatinine levels were significant high ($p<0.001$) in control group (gentamicin) in comparison to those of baseline control. These levels were significantly diminished ($p<0.01$) in the experimental group (*Ashwagandha* and gentamicin) when compared to those of control group (gentamicin)[17].

***Yavasa*:** *Alhagi pseudalhagi (Zygophyllaceae)* known as *Yavasaka* in Sanskrit is a small thorny shrub having a significant effect on the rate of stone expulsion[18].

Shigru*:** *Moringa oleifera* ***(*Moringaceae)* is a potent diuretic and found very effective in the management of Urinary tract infection.

Haridra :- *Curcuma longa (Zingeberaceae)*:- One study showed that *Haridra* has nephroprotective and diuretic action along with *Petroselinum sativum, Eruca sativa* which were examined in gentamicin induced nephrotoxicity in rats. The results showed that gentamicin induced nephrotoxicity get improved by oral administration of aqueous infusion of these three drugs in combination[19]. Curcumin and Rutin are polyphenolic compounds present in *Haridra* are very good antioxidant and anti-inflammatory. Addition of rutin and curcumin normalizes and restore raised levels of calcium oxalate in urine and kidney near to normal and showed minimum tissue damage in kidney of animal treated with those two compounds as compared to calculi-induced animal.

This effect is mediated possibly through a lowering of urinary conc. of stone forming anti-inflammatory, constituents, and antioxidant effects[20].

Manjistha:- *Rubia cordifolia (Rubiaceae)* –Some researches have shown that hydro-alcoholic extract of *Manjistha* was investigated in nephortoxicity induced by Cisplatin albino mice. Cisplatin was administered intraperitoneally to one set of mice while another set of mice were given hydro-alcoholic extract of *Manjistha* at different doses along with cisplatin. The extract significantly decreased the cisplatin induced nephrotoxicity[21].

Brihat Gokshura: *Pedalium murex (Pedaliaceae)*:- In a study Nephrotoxicity was induced in rats by administering Cisplatin 5mg/kg intraperitoneally and effect of administration of *Pedalium murex* ethanolic extract was determined using serum creatinine, blood urea and change in body weight as indicators of kidney damage. Cystone was taken as a standard drug. The results have shown that the ethanolic extract of *Brihat Gokshura* has a remarkable nephroprotective action as compared to cystone[22].

Sahadevi :- *Vernonia cinerea (Asteraceae)* - alcoholic extracts of aerial parts of Vernonia cinerea has been examined for its effect on Cisplatin induced nephrotoxicity in albino rats. The alcoholic extract showed distinct therapeutic action and the ethyl acetate extract has shown a very good prophylactic action and petroleum ether extract exhibited moderate safety for both therapeutic and prophylactic action in cisplatin-induced toxicity[23].

Pashanbheda:- *Aerva lanata (Amaranthaceae)*- *Pashanbheda* is very good nephroprotective drug with very less toxicity and offers an encouraging role in the treatment of acute renal failure. In one study the ethanolic extract of *Pashanbheda* whole plant was studied for its nephroprotective action in acute renal injury by inducing Cisplatin and Gentamicin in albino rats[24].

Shunthi:- *Zingiber officinale (Zingiberaceae)*- Nephrotoxicity was induced by i.p. administration of gentamicin 100 mg/kg for eight days in rats. Gentamicin-induced glomerular, peritubular and blood vessel congestion and accumulation of inflammatory cells of the kidney were reduced in the groups taking the ethyl acetate and dried extract of fresh *Zingiber offiicinale* along with gentamicin[25]. One study shows that Ginger has an antioxidant action which reduces oxidative stress in the body. Administration of its ethanolic extract to ethylene glycol rats prevented saturation of coax and decreases their deposition in renal tubules[26].

Haritaki:- *Terminalia chebula (Combretaceae)* - The extract of *Terminalia chebula* has been known to have uremic toxin decreasing action in rats. It decreases the blood urea nitrogen, serum creatinine and guanidinosuccenic acid significantly[27].

Sariva:- *Hemidesmus indicus linn (Apocynaceae)***:** Sariva assisted in the treatment of kidney damage. The plant shows promise as an aided treatment together with aminoglycosides as it diminishes nephrotoxicity caused by aminoglycosides[28].

Makoy:- Solanum nigrum (solanaceae**)** - Makoy have significant nephroprotective activity. Nephrotoxicity was induced in rats by i.p. administration of gentamicin. Effect of simultaneous administration of extract of fresh *Makoy* orally was determined using S. creatinine, B. urea, AST, ALT, ALP and protein as indicators of kidney damage. The fresh juice extract of *Makoy* significantly protected rat kidneys from gentamicin-induced nephrotoxicity[29].

Gokshura :- *Tribulus terrestris (Zygophyllaceae)*- It's different parts has a range of chemical constituents, which are therapeutically vitals like flavonoids, flavonol glycosides, steroidal saponins, and alkaloids. It is a very good diuretic, antiurolithic and immune-modulator drug. Many researches have been done to ascertain biological actions and pharmacology of extracts of *Gokshura*.

One study illustrated that the aqueous extract of *Gokshura*, in oral dose of 5 g/kg, elicited a positive diuresis, which was slightly more than diuresis by furosemide. The increased tonicity of the smooth muscles, which was produced by *Gokshura* extract, together with its diuretic action supported in the expulsion of stones[30]. Anothers study shows that in which evaluation of different extracts of *Gokshura*, such as aqueous, methanolic, high strength *Kwatha*, low strength *Kwatha* and *Ghana* powder for diuretic action in albino rats. High strength *Kwatha* exhibited diuretic action comparable to that of control drug Furosemide[31].

In one study, ethanolic extract of *Gokshura* was tested in urolithiasis induced by glass bead implantation in albino rats. It exhibited significant safety against deposition of calculogenic material around the glass bead and serum urea levels. Subsequent fractionation of the ethanol extract led to a decrease in activity[32].

***Yava*:-** *Hordeum vulgare* (poaceae)- It contains flavonoid i.e.-saponarin. Saponarin on hydrolysis gives equilibrium mixture of saponaretin & vitexin, which are responsible for its antioxidant effect. Ethanolic extract of *Yava* significantly

reduced the urinary excretion of urea, calcium, magnesium, phosphate, uric acid and oxalate and increased excretion of citrate compared to EG control. It was also noticed that the treatment with *Yava* produced significant decrease in lipid peroxidation and increased levels of superoxide dismutase and catalase and concluded that urolithiatic effect is due to antioxidant activity[33].

CONCLUSION

Considering all the available evidence, this review presents that drugs causing urolithiasis have multiple mechanisms of action including- Diuresis, Lithotriptic, Alteration in physiological pH, Antioxidant activity, Inhibition of oxalate synthesizing enzymes and some drug often shows more than one mechanism of action. Treatment on the basis of modern medicines is often having risk of side effects, low efficiency and is often too expensive. This review article is an attempt to compile the reported mechanism and chemical constituent of different ayurvedic herbal drug which may be responsible for its therapeutic and traditional use in urolithiasis. Although these herbal medicines are popular in folk culture but detail fingerprint and rational of safety & efficacy of these herbal medicine is not well established. Precise observation of action of this herbal medicine has great importance in the development of safe & effective antiurolithiatic drug and it may be useful to the medical researchers, scientists and scholars working in the paradigm of pharmacology and therapeutics to inculcate evidence-based alternative medicine to cure urolithiasis without any adverse toxic effects and also to reduce the chances of stone recurrence. It offers the principal foundation for forthcoming research on application of transitional, preventive and personal medicinal plants.

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