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NEPHROPROTECTIVE EFFECT OF "*NEPHROWIN*" *ARKA*: A SYSTEMATIC REVIEW OF AYURVEDA POLYHERBAL FORMULATION

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ABSTRACT

The rise in the ageing population, non-communicable diseases, exposure to air pollution, various chemicals in everyday life, and changes in dietary habits, such as consumption of junk food, sugary beverages, and a sedentary lifestyle, significantly contribute towards progressive cumulative renal injury. Over the years, it has been recognised as a risk factor for the development or worsening of chronic kidney disease. However, there remains a lack of safe and effective drugs to reverse or stabilise renal function. In preview of the above-mentioned conditions, KRM Ayurveda has introduced the drug, *Nephrowin Arka*, comprising 3 Ayurveda herbs- *Punarnava, Kasni, Makoy* to manage the disease condition by improving kidney functions, GFR (Glomerular Filtration Rate) and rejuvenating the nephrons. The dosage form was chosen as *Arka Kalpana* (distillation method), as it is easy to administer to patients with *Mridu Prakriti* (tender nature). An in-depth literary review was done, which summarised evidence-based knowledge traditionally used for CKD management, amalgamating the ancient aspect which elucidated its *Agni Deepak*(Increasing digestive fire), *Tridoshaharahar*(Pacifying three bodily energies), *Vishaghna*(detoxifying), *Mutral*(increasing urine output), *Shothahara*(decreasing swelling), *Rasayan*(Rejuvenating) properties along with contemporary aspect corroborating the above said by signifying its antioxidants, analgesic, nephroprotective, diuretic and immunomodulatory effects quintessential in the management of CKD.

Keywords: CKD (chronic kidney disease); Nephroprotective; Herbs; Rejuvenation.

INTRODUCTION

The World Health Organisation projects that chronic kidney disease will become the 5th most common chronic disease by 2040. Causes of CKD are multifactorial and diverse.[1] The rise in the ageing population and non-communicable diseases like Diabetes mellitus and Hypertension are significant contributors as risk factors for renal injury.[2] Exposure to the changing environmental factors, i.e. air pollution, exposure to various chemicals in everyday life, affects renal function. It contributes towards progressive cumulative renal injury over a lifetime, acting as a risk factor for developing or worsening chronic kidney disease. Studies have shown that exposure to PM10 and PM2.5 (particulate matter) is associated with a reduction in eGFR.[3]. Apart from environmental changes, individuals' dietary habits have also changed, with the consumption of sugary beverages, packed snacks, cookies, breads, buns, confectionery, pizza, pasta, etc., becoming an integral part of their daily routines. A linear relationship is observed between ultra-processed food intake and risk of CKD. [4] Junk food consumption is inescapable in youngsters; hence, the incidence of CKD is likely to increase in children. But there remains a lack of safe and effective drugs to reverse or stabilise renal function in patients with glomerular or tubulointerstitial causes of CKD [5]

In line with the above-mentioned conditions, Karma Ayurveda has introduced *Nephrowin Arka* to manage kidney disorders. *Arka Kalpana* (distillation) was prepared with due consideration, as it is easy to administer to patients with *Mridu Prakriti* (tender nature) who are hesitant to take medicines such as *Churna* (powder), *Kwath* (decoction), etc. *Arka*, being *Laghupaki* (easily digestible), *Vyavayi* (spread in the body before digestion), and *Vikasi*, assimilate quickly in the body and has good palatability. [6] This article aims to highlight the nephroprotective effects of the polyherbal medicine *Nephrowin*.

Materials and methodology

The drug selected for the review is *Nephrowin Arka*, manufactured by KRM Ayurveda, Kundali, Haryana. In depth review was done considering The Textbook of *'Bhavaprakasha Nighantu'* by Acharya *Bhavamishra*, Textbook of 'Reviews on Indian Medicinal Plants' by ICMR, The Ayurvedic Pharmacopoeia of India by Government of India, Ministry of AYUSH, The Ayurvedic Formulary of India by Government of India, Ministry of AYUSH, published research articles in different journals available online, various databases and search engines.

Observations & Result

Arka Nephrowin consists of a combination of the following 3 Ayurvedic herbs: *Punarnava, Kasni*, and *Kakmachi/Makoy*. The detailed description is mentioned below in Table 1:

S. No.	Name	Botanical Name	Part used	Qty.
1	*Punarnava*	*Boerhaavia diffusa*	Root	0.6 g
2	*Kasni*	*Cichorium intybus*	Seed	0.6 g
3	*Kakmachi*	*Solanum nigrum*	Whole Plant	0.6 g
4	Water	-	-	28.8 ml

The herbs selected for this formulation contain active constituents that exhibit nephroprotective activity. Classical texts of Ayurveda have also mentioned these drugs, either as single herbs or in combination, for the treatment of various nephrological conditions, such as *Mutrakricha, Mutrakshaya*, etc., arising from *Vataja dosha*. Also, mutiple pharmacological, experimental, and clinical screenings have shown that these herbs exhibit various properties that make them useful nephron-protective agents. After screening classical texts, the following biological properties of the ingredients were found, as described in Table 2.

S.no.	Ingredient	Classical Property
1.	*Punarnava*	*Agni Deepak*(increasing digestive fire), *Vatakaphahar*(*vata kapha dosha* pacifying), *vishaghna*(detoxifying), *Mutral*(diuretic), *Shothahara*(reduces swelling), *Rasayana*(rejuvenating).[7]
2.	*Kasni*	*Pittashamak* (pita dosha pacifying), *Kupachan*(improves digestion), *Shothahara,Mutrakricha*(dysuria)[8]
3.	*Makoy*	*Mutral, Tridoshahara, Rasayan* [9]

The presence of multiple active phytoconstituents in the ingredients of Nephrowin Arka helps confer various desirable biological activities. Description of properties after analysis is described in Table 3.

S.no.	Ingredient	Biological Activity	Study Details
1.	*Punarnava*	a) Diuretic	Phytochemical evaluation for the extract was performed using standard procedures. Results showed that single-dose administration of the alcoholic extract of *Boerhaavia diffusa* roots at 100, 200, and 300 mg/Kg, and the standard Furosemide (10 mg/kg), increased urinary output, along with increased concentrations of Sodium, Potassium, and Chloride ions in urine. The alcoholic extract of the roots of *Boerhaavia diffusa* showed greater diuretic activity, comparable to that of the standard Furosemide (10 g/kg).[10]
		b) Antioxidant	In vitro, studies of the hydro-alcoholic extract of *Boerhavia diffusa* depicted free radical scavenging activity. [11] *Boerhavia diffusa* extract significantly protects against hyperoxaluric oxidative stress and renal cell injury in urolithiasis in the rat kidney. [12]
		c) Renoprotective	A study was performed on 20 mixed-breed dogs of mixed breeds suffering from CRF(Chronic renal failure) from 1 to 2 months, they were divided into two groups ($n = 10$), Group I treated with Enalapril at 0.5 mg/kg once daily for 90 days; Group II treated with *Boerhavia diffusa* root extract at 500 mg daily for 90 days. In both treatments, serum creatinine, urea nitrogen, phosphorus, urinary protein, ALP, and GGT showed significant ($P < 0.05$) reductions by day 60. However, potassium levels were normalised only with the *Boerhavia diffusa* root extract treatment by day 30. [13] In another study, *B. diffusa* extracts were tested for diuresis and renal enzymes in toads. They exhibited diuretic activity and also stimulated kidney d-amino acid oxidase activity. (Chowdhury and Sen, 1955).[14]
		Anti-inflamatory	Boeravinone B (6) exhibited significant anti-inflammatory activity (56.6% at 50 mg/kg) when evaluated in an in vivo carrageenan-induced rat paw model. [15] In another study, root extract was evaluated for pyelonephritis in rats, which showed a reduction in inflammatory changes and abscess formation in the kidneys of animals inoculated with E. coli, and also reduced bacterial counts in urine samples from infected animals (Singh et al., 1988).[16]

2.	*Kasni*	Renoprotective	In vitro and in vivo biochemical experiments showed that chicory acts on the renal uric acid transporter GLUT9, downregulating its protein expression to reduce uric acid. [17]
		Antioxidant	The methanol extract of the plant showed inhibition of lipid peroxidation, hydroxyl scavenging activity and superoxide radical generation. The concentration for 50 per cent inhibition was 0.88 mg/ml, 0.08 mg/ml and 0.1 mg/ml for the three activities, respectively (Joy and Kuttan et al., 1995). The 95 per cent ethanolic extract of leaves demonstrated concentration-dependent (10 and 200 g/ml) inhibition of DNA sugar damage (up to 55 per cent) in the reaction mixture containing calf thymus DNA and free radical-generating system (Sultana et al., 1995). The extract of leaves and dried leaf powder showed marked inhibition of lipid peroxidation estimated in vitro in goat liver homogenate (Saroja et al., 2000-2001).[18]
		Anti-inflammatory	Aqueous extract or root produced greater anti-inflammatory action than alcoholic extract in the formalin-induced rat paw oedema model (Jindal et al., 1975).[19]
3.	*Makoy*	A) Analgesic	The analgesic and anti-inflammatory activity of the ethanolic extract of the fruits of the Solanum nigrum plant was evaluated by using Carrageenan-induced rat paw oedema. In contrast, the analgesic activity of the extract was evaluated for its central and peripheral pharmacological actions by using Eddy's hot plate and acetic acid-induced writing. The extract showed significant analgesic and anti-inflammatory activity at a dose of 500 mg/kg compared with the standard drug Diclofenac sodium (50 mg/kg).[20]
		b) Antioxidant	*S. nigrum* aqueous leaf extract modulates restraint stress-induced Changes in rats, thereby combating oxidative stress-induced damage.[21]
		c)Anti-inflammatory	The effect of methanolic extracts of berries of *Solanum nigrum* was studied on carrageenan-induced paw oedema. Methanolic extract decreased oedema in the hind paw. The methanolic extract of *Solanum nigrum* has shown significant anti-inflammatory activity. In another study, nine new steroidal saponins, solanigrosides Y1-Y9, together with seven known congeners, were isolated from the berries of *S. Nigrum*, which depicted potential inhibitory effects on nitric oxide and IL-6 production induced by lipopolysaccharide in a macrophage cell line. The compound exhibited a significant reduction in NO production and IL-6 levels, indicating significant anti-inflammatory activity. [22,23]

Clinical Evidence

Punarnava(*B. Diffusa*) was used in a double-masked trial to study the effect of '*Punarnava*' (plant) on haemoglobin, blood urea, serum cholesterol, blood sugar, vital capacity and body weight in 43 regular healthy adult volunteers in the age group 45-50 years over a period of 42 months. It did not show any ap-

preciable effect on the blood constituents in the initial examinations. Subsequent examinations have shown that it decreased blood urea and serum acid phosphatase with an increase in serum cholesterol and a marginal increase in blood sugar. Weight remained almost stationary (Appa Rao et al., 1967, 1969).[24]

Another clinical trial supports its diuretic action. In a trial involving 19 patients with generalised anasarca (jaundice of varying aetiology), plant root extract was given orally, and urine output and pulse rate were recorded. In subsequent weeks, urinary output increased, with a reduction in urine specific gravity. The effect was more marked in cases of anasarca due to renal cause and anaemia. Whereas there was no use in cases of ascites due to cirrhosis of the liver (Basu, 1910). [25]. Chopra et al. (1923) studied the diuretic effect of the plant extract in 34 cases of oedema of varying origins. It produced diuresis in cases of obesity and ascites, especially those due to early liver, peritoneal and kidney conditions. The drug had a more marked effect in certain types of cases of ascites, i.e. those due to early cirrhosis of the liver and chronic peritonitis, than some of the other known diuretics.[26]

In a controlled clinical trial of 15 cases of nephrotic syndrome (including 3 in the control group), a decoction or a total crude powder (10 g daily in divided doses) showed beneficial effects comparable to those of corticosteroids. Of the 12 cases treated with decoction, 4 showed relief, 7 improved, and 1 deteriorated. It was observed that in cases of nephrotic syndrome, the decoction induced a notable degree of diuresis. The diuresis was slow but prolonged. Besides relief of clinical oedema, these patients also showed overall improvement, including a decrease in albuminuria and an increase in serum protein (Singh & Udupa, 1972d). [27]

It depicted an immunomodulatory effect. A clinical study was conducted to evaluate the diuretic and immunomodulatory actions of '*Punarnava*' with special reference to nephrotic syndrome in 40 patients. The drug was administered to patients at a dose of 500 mg thrice a day for one month. The results showed increased serum protein levels and reduced urinary protein excretion in patients with nephrotic syndrome. An increase in immunoglobulin and immunocomplex levels was also noted after one month of medication. (Singh et al., 1992).[28]

DISCUSSION

Due to changes in diet and lifestyle, and increasing atmospheric pollution, kidney diseases are rising at an alarming rate. Studies show that long-term exposure to atmospheric pollutants is associated with decreased eGFR and increased prevalence of chronic kidney disease (CKD). Mechanisms likely involve oxidative stress and inflammation in the body.

Kidney patients may present with symptoms such as hematuria, foamy urine, nocturia, flank pain, or decreased urine output. If CKD is advanced, patients may report fatigue, poor appetite, nausea, vomiting, metallic taste, unintentional weight loss, and pruritus, changes in mental status, difficulty in breathing, or swelling of the body.[29]

Numerous herbs have rejuvenating effects on the kidneys and hence depict nephroprotective action. Keeping this in mind, "*Arka Nephrowin*" was formulated. *Arka* was chosen as the dosage form because it has detoxifying effects on the body, aids digestive fire, and is more palatable than *curna* or *kvatha Kalpana*. Punarnavine, which is an alkaloid present in the root of the plant and secondary metabolites such as rotenoids, ecdysteroids, alkaloids, and phenolic and lignan glycosides account for its various pharmacological activities.[30] The plant's diuretic action was demonstrated by beta-ecdysone isolated from the root. (Suri et al., 1982). Another study depicted three polyphenols, such as rutin, syringic acid, and epicatechin, determined through the RP-HPLC-PDA method, are found to be maximum in root extract. Responsible for describing potential against free radicals. [31] The total phenolic and total flavonoid contents of C. intybus seed extract contribute to its antioxidant activity. [32] . Chicoric acid, present in Cichorium intybus (chicory) seeds, accounts for its anti-inflammatory activity.[33] *S. nigrum* depicts antioxidant potential by depicting protective effects against CCL4, which affects the kidneys,

causing acute tubular necrosis and decreased glomerular mass.[34]

CONCLUSION

In this paper, we have provided a brief review of the proprietary Ayurvedic medicine Nephrowin Arka, which contains herbs such as Punarnava, Kasni, and Makoy. The review summarised evidence-based knowledge traditionally used for CKD, amalgamating the ancient aspect, which stated its *Agni Deepak*, *Tridoshaharahar*, *Vishaghna*, *Mutral*, *Shothahara*, *Rasayan* properties, along with the contemporary aspect, corroborating the above by signifying its antioxidants, analgesic, nephroprotective, diuretic and immunomodulatory effects quintessential in the management of CKD.

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