



Nephroprotective activities of Raktapunarnavā (*Boerhavia diffusa* L.) – An Ayurvedic Rejuvenative Drug: A Review

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ABSTRACT

Raktapunarnavā (*Boerhavia diffusa* L.) is an important Ayurvedic rejuvenative drug, widely used to treat various ailments associated with the diabetic, respiratory system, urinary system, hepatic system, cardiovascular system, etc. Recent studies have proven potential as a natural remedy for managing chronic kidney disease. This review highlights the nephroprotective activities of *B. diffusa* against renal damage caused by various drugs, chemicals and other disorders.

Keywords: Raktapunarnavā, Boerhavia diffusa, nephroprotective effect, chronic kidney disease, polyphenols, antioxidant.

INTRODUCTION

idneys are main emunctory organ facilitated to play crucial physiological functions in infiltration, excreting metabolite waste and toxins from the blood and maintaining the electrolyte in the body's fluid. Generally kidneys are subacted with various drugs and toxins aggressions, which lead to many complications against normal functions of the kidney. When the kidneys are impaired, the body cannot effectively excrete urine and waste, leading to increased levels of urea, uric acid, creatinine and electrolytes in blood. Chronic kidney disease (CKD) is a global health issue that affects mostly adults and is increasing in both developed and developing countries. Chronic renal injury as initiated by CKD is characterized by a variety of clinical symptoms including renal detoxification potential loss, water-electrolyte metabolism disruption, acid-base equilibrium disturbance, and endocrine imbalance. Predominantly patients with diabetes and hypertension are highly susceptive to develop progressive renal damage and CKD in future. Cardiovascular disease is a major cause of increased morbidity and mortality in patients with CKD. The conventional management approach includes dialysis and renal transplantation involving high costs and complexity and unaffordable for the ordinary person in India. Therefore, it is necessary to explore safe and cost-effective treatments.¹⁻⁴

"Punaŗnavā" is an important traditional Ayurvedic rejuvenative drug, has gained attention for its potential in managing CKD. It stimulates the function of heart and kidney and is specific for jaundice, diabetes, general debility and other diseases caused by kapha and pitta. In Ayurvedic texts two varieties of *Punaṛnavā* viz. *Raktapunaṛnavā* (red variety) and *Śvētapunaṛnavā* (white variety) are mentioned. *Raktapunaṛnavā* is invariably equated with *Boerhavia diffusa* L. (Family – Nyctaginaceae), commonly known as Spreading Hogweed in English, Mookarattai keerai in Tamil and Tavilama or Talutama in Malayalam. It is a perennial herb; stems trailing, to 200 cm; glabrous or sparsely pubescent; roots thick, fleshy. Petiole 0.4 -2 cm; leaf blade ovate, $1-5 \times 1-4$ cm, both surfaces sparsely pubescent, abaxially gray-yellow, wrinkled when dry, base rounded or cuneate, margin undulate, with stout, muticellular hairs, apex obtuse or acute. Inflorescences terminal, capitatecymose panicles; peduncle slender, sparsely pubescent. Pedicel short to almost absent. Perianth limb bright purple or purple-red, 1.5-2 mm. Stamens 1-3(-5), slightly exserted or included. Anthocarp clavate, 3-3.5 mm, 5-ribbed, with viscid glands, apex rounded.⁵

In Ayurveda, it is considered to be light (Laghu), dry (Ruksha) and hot potency (Ushna veerya) and the properties like: Rasa - Madhura, Tikta, Kashaya; Veerva - Ushana; Vipaka – Madhura; Karma - Anulomana, Shothahara and alleviate all three doshas.⁶ The plant is anthelmintic, diuretic, bitter, astringent, cooling, aphrodisiac, cardiac stimulant, diaphoretic, emetic, expectorant, anti-inflammatory, febrifuge and laxative besides being an active ingredient as a tonic. The root, leaves and aerial parts are abundantly used as the potential folk medicinal regimen to treat various ailments associated with the respiratory system, urinary system, hepatic system, cardiovascular system, etc. It is useful in all types of inflammation, strangury, leucorrhoea, ophthalmia, lumbago, myalgia, cardiac disorders, jaundice, anaemia, dyspepsia, constipation, cough, bronchitis and general debility. The leaves are used for treatment of jaundice, liver complaints, hypotension, skin diseases, night blindness and also used as an antidote to snake poisoning. Similarly roots are useful for gonorrhoea, dropsy, bronchial asthma, night blindness, rheumatism, several diseases of urine, liver, kidney and heart.⁷⁻¹³ This herb works extremely effectively on the urinary system and directly targets the damaged nephrons caused by high blood sugar level in diabetes. It improves kidney filtration and flushes away extra fluids and waste.¹⁴ This review presents the evidence-based protective effects of B. diffusa against renal damage caused by various drugs, chemicals and other disorders.



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Figure 1: Shoot



Figure 2: Root

MATERIALS AND METHODS

Relevant original research and review articles were considered, and the mentioned aspects were collected and compiled. Extensive literature search on the nephroprotective properties of the whole plant or the parts of *B. diffusa* was conducted using specialised and dedicated search engines and websites like Google Scholar, PubMed, ScienceDirect, Sci-Hub, SciFinder, etc.

Nephroprotective activities of Boerhavia diffusa (BD):

Pareta et al., investigated the protective effect of aqueous root extract of BD (200 - 400 mg/kg/day) in acetaminophen induced nephrotoxicity in rats. Administration of acetaminophen (200 mg/kg/day) for 14 days to rats induced marked detritions of renal function, characterized by a significant (P<0.01) increase in blood urea nitrogen, serum creatinine and injured the renal cells evident from increased level of kidney malondialdehyde (MDA), protein thiol along with depletion of super oxide dismutase, catalase, glutathione peroxidase activities and reduced glutathione levels. However pre-treatment with BD root extract protected against these changes. Histopathology also showed that acetaminophen caused significant structural damages to kidneys like tubular necrosis, degeneration of epithelial cells, glomerular damage and congestion which were reversed with BD root extract. Their results suggest that BD has the potential in preventing the acetaminophen-induced nephrotoxicity.¹⁵

Pareta et al., also evaluated the ameliorating effect of aqueous root extract of BD in hyperoxaluric oxidative stress and renal cell injury in rat kidney. They found that the BD root extract possess high polyphenolic content and exhibited significant free radicals scavenging activity. BD treatment significantly increased oxalate excretion and reduced level of malondialdehyde (MDA) and improved the activity of antioxidant enzymes followed by reduction in blood urea nitrogen (BUN) and serum creatinine. Furthermore, it also reduced the number of CaOx monohydrate crystals in the urine.¹⁶

Prem Kumar Singh et al., observed the increased levels of serum markers of kidney function, and reduced Na⁺-K⁺ ATPase activity and endogenous antioxidant status in alloxan induced diabetic rats. Administration of ethanolic extract of BD (500 mg/kg b.w. for 30 days) not only maintained the ionic balance and renal Na⁺-K⁺ ATPase activity and the renal antioxidant status (GPx, Catalase, SOD and GSH) remained in the near normal range. The study provides evidence for BD to be a potent renoprotective and antihyperglycaemic agent in diabetic animals.¹⁷

The nephroprotective effect of BD leaves ethanolic extract (200 and 400 mg/kg b.w.) against Cisplatin (5 mg/kg b.w.) induced toxicity was analysed in Wistar rats by measuring the levels of SOD, CAT, LPO, Vitamin-C, TRG, GPx, GR and GST. The serum was taken to assess the levels of urea, uric acid, total protein, albumin, creatinine, blood urea nitrogen and electrolytes. The results revealed that the BD extract possess nephroprotective activity against Cisplatin induced nephrotoxicity. The leaves extract had the ability to normalize the elevated levels of urea, creatinine, uric acid, BUN in serum and LPO in kidney and improved the antioxidant levels. Higher dose of ethanolic extract (400 mg/kg b.w.) showed more protective effect than lower dose and concluded that the nephroprotective effect of BD could be attributed to its free radical scavenging efficacy.¹⁸

The alcoholic extract of BD root was evaluated on ethylene glycol-induced lithiasis in rats. Administration of ethylene glycol for 28 days increased the concentration of calcium, phosphate ions, uric acid and oxalate in urine, consequently renal stone was formed. Treatment with BD root extract (250 & 500 mg/Kg) significantly (P<0.05) reduced the elevated levels of these ions in urine. The histopathological studies confirmed the reduced level of degenerated glomeruli, necrotic tubule and inflammatory cells.¹⁹

The protective effect of BD against gentamycin induced renal failure in albino rats was studied by Pramila and Vijay Kumar. Administrations of gentamycin (80 mg/kg. b.wt) for 10 days produced increase in the concentration of serum urea, creatinine, uric acid and shrunken glomeruli and glomerular atrophy was observed in histopathology. Posttreatment with *B. diffusa* extract (400 and 800 mg/kg.bwt) for 9 weeks exhibited anti-nephrotoxic effects (restorative) against degenerative changes of renal cortical architecture



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and also significant normal values of serum urea, creatinine and uric acid levels.²⁰

Similar experiment also carried out by Sawardekar and Patel to evaluate the effect of aqueous root extract of BD in gentamicin induced nephrotoxicity in rats. Administration of gentamicin sulfate (150 mg/kg for 10 days) induced acute kidney injury as evidenced by a significant increase in blood urea nitrogen, serum creatinine, kidney malondialdehyde, and glutathione when compared to normal control. Pretreatment with α -lipoic acid (ALA) (25 mg/kg for 10 days; positive control) maintained the serum creatinine and blood urea nitrogen levels comparable to normal control group. Treatment with BD root extract (200 and 400 mg/kg/day) prevented the changes in above parameters and comparable to ALA. Effects of both doses of BD were significantly (P<0.05) better than gentamicin induced group and concluded that BD exerted protection against structural and functional damage induced by gentamicin possibly due to its antioxidant properties.²¹

Sarita et al., evaluated the comparative nephroprotective effects of Ficus religiosa (stem bark), Tinospora cordifolia (stem), Moringa oleifera (leaves) and Boerhavia diffusa (roots) on gentamicin-induced nephrotoxicity in albino Wistar rats. Hydro-alcoholic extracts of above plants were used at two doses levels of 200 & 400 mg/kg respectively. Gentamicin only treated animals showed significantly (P < 0.001) increased urine creatinine, serum urea, and blood urea nitrogen; whereas cordifolia and B. *diffusa* hydro-alcoholic Τ. extracts treatment reversed the effect of gentamicin toxicity indicating nephroprotective activity in compared to other plant extract treated animals. Furthermore, higher dose of hydro-alcoholic extract (400 mg/kg) of T. cordifolia and B. diffusa contains rich in flavonoids and polyphenolics which are responsible for potential nephroprotective activity in gentamicin-induced nephrotoxicity in rats.²²

The efficacy of aqueous leaves extract of BD on mercuric chloride (HgCl₂) induced nephrotoxicity in male Wistar rats was evaluated by Indhumathi and co-workers. HgCl₂ (200 μ g/kg b.w. for 10 days) treated animal group showed increased in serum ALP, acid phosphatase, aspartate transaminase, ALT, LDH, LPO, urea and creatinine. But the group treated with HgCl₂ followed by leaves extract (200 mg/kg/day for 10 days) showed that there was reversal of above parameters and increased levels of GPx.²³

Oburai et al., conducted a comparative clinical evaluation of enalapril standard drug (0.5 mg/kg; group – I) and BD root extract (500 mg; group – II) in chronic renal failure (CRF) dogs for 90 days. It was observed that the CRF dogs showed a significant (P<0.05) increase in systolic and diastolic blood pressure, serum creatinine, urea nitrogen, sodium, potassium, phosphorus, urinary protein, alkaline phosphatase (ALP), glutamyl transferase (GGT) and significant (P<0.05) decrease in hemoglobin and total erythrocyte count (TEC). Nephrosonography revealed indistinct corticomedullary junction, altered renal architecture, hyper-echoic cortex, medulla, and sunken kidneys. But both treatments (group – I and II) exhibited significant (P<0.05) reduction in systolic and diastolic blood pressure in 30 days and serum creatinine, urea nitrogen, phosphorus, urinary protein, ALP, and GGT reduction in 60 days. Though, the potassium level was normalized only in BD treated group in 30 days and they concluded that the efficacy of BD root extract was comparable to standard enalapril treatment of CRF in dogs.²⁴

The prophylactic and curative effect of BD leaf ethanolic extract on kidney damage induced by fluoride in rats was studied. Treatment with sodium fluoride (300 and 600 ppm /kg bw/day) for 40 days exhibited the level of malondialdehyde (MDA) significantly (p<0.001) increased while glutathione (GSH) and activities of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) were significantly (p<0.001) decreased. Pre and post-treatments with BD L. leaf extract (500 mg/kg bw/day) for 20 days showed significantly (p<0.001) enhanced antioxidant enzymes activities of SOD, CAT and GPx in rats kidney tissue. The significant higher nephroprotective effect was observed in pre-treatment with BD leaf extract than post-treatment in sodium fluoride treated rats.²⁵

The effect of leaves ethanolic extract of BD on renal functions in streptozotocin (STZ) (60 mg/kg b.w.) induced diabetic rats was evaluated. There was a significant increase in the levels of serum urea, uric acid and creatinine in STZ induced rats when compared with the normal rats. Administration of BD leaves extract (500 mg/kg b.w.) for 45 days showed a significant decrease in the levels of serum urea, uric acid and creatinine when compared to STZ induced diabetic rats. Thus showing that BD leaves extract improved renal morphology and function in STZ conditions.²⁶

Kalaivani et al., evaluated the protective effect of ethyl acetate fraction of BD on cell damage induced by cyclosporine in Madin–Darby Canine Kidney cells. Results showed that BD protected the cells from cyclosporine-induced apoptosis and cell cycle arrest through its antioxidant potential by the polyphenolic compounds.²⁷

A case study by Suman Kundu reported that a patient was known hypertensive and non-diabetic (53 years male) came to Kayachikitsa OPD of Raghunath Ayurved Mahavidyalaya & Hospital with chief complains of elevated urinary protein in yearly routine investigation. He was taking a combination of two antihypertensive drugs amlodipine (5 mg) along with atenolol (50 mg) for last 4 years regularly. After clinical diagnosis the following results were found - Urine RE/ME showing trace albumin in 24 hr urine, Fasting blood glucose - 89 mg/dl, Spot urine albumin creatinine ratio - 77.5 µg/mg of Creatinine, BUN Creatinine ratio - 7.91, e-GFR - 99 mL/min/1.73 m². Only single oral drug therapy with Punarnava churna (BD) was advised to patient at the dose of 1.5 g thrice daily with normal water and the conventional antihypertensive drugs were advised to continue. Patient was evaluated by the biochemical markers of kidney damage in a regular interval for more than two months and



the followings results were observed. Spot urine albumin creatinine ratio - 13.5 μ g/mg of Creatinine, BUN Creatinine ratio - 8.72, e-GFR - 105 mL/min/1.73 m² and concluded that BD has been found to alleviate the markers of renal injury without any remarkable changes in blood pressure via antioxidant mechanism.¹

Vidhi Sharma et al., evaluated the diuretic activity of BD root extract in rats. The results showed that single dose administration of root alcoholic extract of BD (100, 200 & 300 mg/Kg) and standard Furosemide (10 mg/kg) have increased the urinary output along with an increase in concentration of Na, K, and Cl ions in urine and concluded that BD root extract produced a greater diuretic activity which is comparable to that of Furosemide.²⁸

In vivo studies on nephroprotective effect of the Boerhavia diffusa (BD) and Tinospora cordifolia (TC) herbal combination was evaluated against Diclofenac (DCF) induced nephrotoxicity in Wistar albino rats in terms of renal biomarkers and inflammatory cytokines estimation, anti-oxidant enzymes status and histopathology. DFC (50 mg/kg b.w./i.p.) treated group showed significant increases in the blood urea, creatinine and uric acid levels while albumin level was found significantly decreased in the blood and urine samples. Herbal combination of BD and TC (162.5 mg/kg/day & 325 mg/kg/day) treated group showed significantly (P<0.05) ameliorated the elevated level of above biomarkers near to the normal in serum and urine. The efficacy of herbal combination treated group was comparable to standard drug alpha keto-analogues (65 mg/kg/day) treatment. Histopathological observations of renal tissues showed impaired renal morphology throughout, with wide Bowman's space, damaged glomeruli, inflammatory cell infiltration and interstitial congestion in DCF treated group. BD, TC combination and standard drug showed a protective effect against the DCF induced toxicity by normalizing the architecture of the kidney tissues and comparable to control group. Thus, it concluded that the herbal combination of the BD and TC were effectively protecting the damages of renal tissues.²

Madhu Singh et al., investigated the therapeutic efficacy of aqueous and alcoholic extracts of roots of Boerhavia diffusa (BD) and leaves of Bryophyllum calycinum (BC) in Wistar rats having chronic kidney disease induced by adenine (200 mg/kg b.w. daily for 28 days). After 28th day, an aqueous and alcoholic extracts of BD, BC (300 mg/kg b.w. daily for 42 days) and bi-herbal combination of aqueous and alcoholic extracts of BC and BD (1:1.5) were given in different groups. Adenine treated group significantly (P<0.05) increased in the serum levels of uromodulin, ALT, BUN, uric acid, creatinine, and phosphorus, with a decreased level of total protein when compared to the normal control group. Administration of either single extract or the co-treatment subsequently with aqueous and alcoholic extracts of BC and BD significantly (P<0.05) restored the biochemical changes by 70th day of the experiment in most of the groups. The effect of bi-herbal combination alcoholic extract was much better in restoring the serum uromodulin and other biochemical values of CKD-induced rats.³

The efficacy of BD in the therapeutic management of cystitis in geriatric dogs was evaluated. BD tablet (1 number per day) and supportive drugs were given to cystitis dogs for 15 days. The efficacy of treatment regimens was measured on day 15 by recording remission of clinical symptoms, haemato-biochemical urinalysis, and biomarkers estimations, ultrasonographical findings and microbiological cure by cultural studies after therapy. Remission in frequency and severity of the clinical signs was noticed from 5th day of therapy among 5 dogs and complete clinical cure among all the 10 dogs was observed by 15th day of the therapy. All the abnormal features of the urine samples of all the affected dogs showed marked improvement from day 7 and normalized by 15th day. The elevated creatinine and BUN values reached to normal range by 15th day of therapy and microbial culture was negative in urine samples from all the affected dogs.²⁹

Martin et al., assessed the antioxidant and potential renal restorative effects of BD root extract on chronic kidney disease. Their experiment revealed that the BD root extract possess renoprotective effects and potentially alleviate CKD progression through its antioxidant properties.³⁰

CONCLUSION

Raktapunarnavā (Boerhavia diffusa) is an important Ayurvedic rejuvenative drug has proven potential as a natural remedy for managing chronic kidney disease. Enormous studies highlight its effectiveness in improving kidney function, mainly through its diuretic properties that helps in flush out excess fluids and waste from the body. It targets damaged nephrons and promote the regeneration of renal tissues. It effectively reduces the serum creatinine, urea, and uric acid levels, promoting an overall improvement in kidney function and the management of chronic kidney disease. Most of the studies reveal that the nephroprotective activity of BD potentially alleviates CKD progression through its antioxidant potential by the polyphenolic compounds. The existing evidence emphasizes its potential therapeutic use and safety as part of a broad strategy for chronic kidney disease management.

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