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Review Article

# Nephroprotective activity of *Boerhavia diffusa*

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ABSTRACT

Nephrotoxicity is one of the most common kidney disorders which occurs when the body is exposed to accumulation of drug or toxin and not able to excrete. A number of therapeutic drugs such as antibiotics, chemotherapeutic agents etc., can weaken the kidney function resulting in acute renal failure, chronic interstitial nephritis, impair the renal function and may also lead to toxicity. The phytochemical review of the plant reveals the presence of many bioactive compounds such as sesquiterpenoids, flavonoids, phenols, steroids and alkaloids with different biological activities. These compounds possess potent nephroprotective properties. The extracts of the plants reviewed exhibited significant dose-dependent nephroprotective and nephron-curative activity.



## 1. Introduction

*Boerhavia diffusa* known as "Punarnava" in Indian traditional system and 'Hog weed' in English, belonging to the family of Nyctaginaceae. Punarnava means one which renews our body and helps to regain the youthness. It was named in honour of Hermann Boerhaave (1668–1738), an Eighteenth century Dutch botanist and the species got the name from typical diffuse branching.[1,2] Boerhavia is distributed widely all along the world. In India, it is available in warmer parts of the country and grows up to 2000 m in the Himalayas and six species are found in India out of 40 i.e., B. diffusa, B. chinensis, B. erecta, B. repens, B. rependa and B. rubicunda. A number of phytochemicals e.g., flavonoids, alkaloids, rotenoids, steroids, triterpenoids, lipids, lignans, carbohydrates, proteins and glycoproteins etc., have been reported from the herb. Several researchers have confirmed phytoconstituents responsible for different activities. Detailed studies on phytochemical constituents have been already reported in previous article.[3]

### 1.1. Nephroprotective activity

Kidney is an important organ which excretes wastes of our body. Nephrotoxicity is one of the most common kidney problems and occurs when body is exposed to a drug or toxin. A number of therapeutic agents can adversely affect the kidney resulting in acute renal failure, chronic interstitial nephritis and nephritic syndrome.[4] Recent reports suggest a vascular origin for most of the diabetic complications including diabetic nephropathy.[5] Several studies have showed effect on nephrotoxicity in animals with significant changes in curing from various drug induced toxicity as well as in dissolving the renal stones. Studies have proved that effect of B. diffusa extract on kidney and diuretic condition. The diuretic activity also attributed to increased sodium excretion rate. Which is due to presence of various

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phytochemicals like glucosides, ecdysone from various parts of plant.[6]

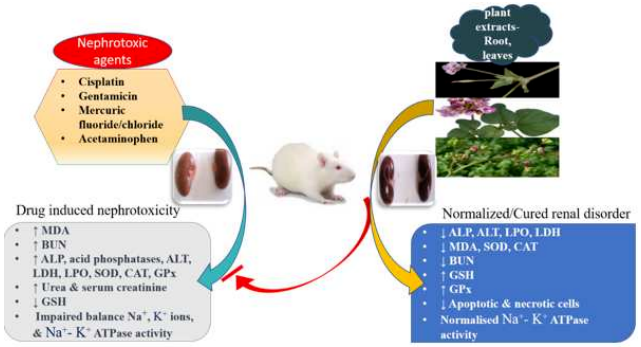


**Fig. 1:** Mechanism of nephroprotective activity of *Boerhavia diffusa* on drug induced nephrotoxicity

### *1.2. Animal studies*

Indhumathi and coworkers found the effect of Aq. leaves extract of B. diffusa on mercuric chloride induced nephrotoxicity in male Wistar albino rats. When a group of rats had induced toxicity (at a dose of 200 mu/kg body wt. for 10 days) there was increase in serum ALP, acid phosphatase, aspartate transaminase, ALT, LDH, LPO, urea and creatinine. The other group of rats were treated with mercuric chloride followed by leaves extract (200 $\mu$/kg/day) for 10 days orally. It is showed that there was reversal of above parameters and increased levels of GPx, increase in reduced GSH, Vit- C and Catalase.[7] Shashi and Kaur elucidated the protective effect of leaf extract of the B. diffusa on kidney damage following fluoride administration in rats. $1^{st}$ Group of rats treated with deionised water orally were treated as control. $2^{nd}$ & $3^{rd}$ group of rats were administered with 300 and 600 ppm of sodium fluoride/kg/day for 40 days. $4^{th}$ group of rats were administered with 500 mg/kg/day of leaf extract for 20 days. $5^{th}$ and $6^{th}$ group of rats were pre-treated with 500 mg/kg/day of leaf extract for 20 days and post exposed to 300 and 600 ppm sodium fluoride/kg/day for next 20 days respectively. $7^{th}$ & $8^{th}$ group of rats were firstly exposed to 300 and 600 ppm sodium fluoride/kg/day for 20 days and then treated with leaf extract for 20 days. It is observed that there was significantly increase in level of MDA and decline in GSH, SOD, CAT and GPx in rats treated with 300 and 600 ppm of sodium fluoride. These results were reverted only when the rats were pre-treated with the extract and post-treated with sodium fluoride ($4^{th}$ group).[8]

Pareta and others studied on acetaminophen induced nephrotoxicity in rats. When toxicity was induced, there was impaired renal function due to increase in BUN, MDA, Serum creatinine and injured renal cells and decreased SOD, CAT, GSH. This was reverted when the rats were administered with Aq. root extract of B. diffusa (200-400 mg/kg/day) and showed the potential against acetaminophen induced renal toxicity.[9]

Sawardekar and Patel Studied the effect of gentamicin induced toxicity in rats. $1^{st}$ group of rats were treated as control which received Distilled water, $2^{nd}$ group of rats were treated as disease control which received gentamicin 150 mg/kg orally for 10 days. $3^{rd}$ group which is positive control received gentamicin 150 mg/kg and 25 mg of ALA orally for 10days. $4^{th}$ and $5^{th}$ groups are treated as test which were given with 200 and 400 mg/kg of leaves extract of B. diffusa respectively. There was increase in body weight in all the group of rats except $2^{nd}$ group over 11 days. High dose of gentamicin caused significant elevation in BUN, serum creatinine and kidney MDA, decreased kidney GSH and histopathological damage in disease control group as compared with normal control. Treatment with B. diffusa prevented changes in above parameters comparable to ALA. Effects of both doses of B. diffusa were significantly better than disease control.[10]

Singh and co-workers studied that there was impaired ionic balance, serum creatinine and $Na^+$-$K^+$ATPase activity in alloxan induced diabetic albino rats. When the ethanolic extract of B. diffusa is administered orally (500 mg/kg for 30 days), it is observed that there was significantly normalization of serum sodium and potassium levels and maintained $Na^+$-$K^+$ATPase activity in the extract treated rats. This shows evidence for B. diffusa to be a potent reno-protective agent in diabetic animals.[11]

Sasikumar and co-workers studied the nephroprotective activity against cisplatin induced toxicity. $1^{st}$group of rats were treated as control (normal rat). $2^{nd}$ group of rats were treated with single dose of cisplatin 5 mg/kg. $3^{rd}$ group of rats (test rats) were treated with cisplatin along with the ethanolic extract (200 mg/kg) for days. $4^{th}$ group of rats (test rats) were treated with cisplatin along with 400 mg/kg of B. diffusa for 4 days. The plant extract had the ability to normalize the elevated levels of urea, creatinine, uric acid, BUN in serum and LPO in kidney. Both the doses of B. diffusa boosted up the antioxidant levels which were found decreased in Cisplatin toxicity. However, the high dose of ethanolic extract of B. diffusa (400 mg/kg) showed more protective effect when compared to the low dose.[12]

### *1.3. Human studies*

Chauhan and co-workers studied the effect of Aq. extract on growth inhibition of crystals (urinary stone) made of Ammonium magnesium phosphate hexahydrate. On administration of 0.5% & 1.0% extracts leads to decrease size of crystal by 50% and complete dissolution is seen in 1% extract. Which is studied using gel-liquid interface method.[13]

Singh and co-workers studied on patients with diabetic nephropathy (with proteinuria >500 mg/day, serum creatinine <0.001) and found that when the punarnava is

**Table 1:** Nephroprotective activity of *Boerhavia diffusa.*

| Extract | Model | Dose | Parameters | Result | |
|---|---|---|---|---|---|
| Aq. leaves extract | HgCl2 induced nephrotoxic male Wistar albino rat | HgCl2-200 mg/kg/d Extract-200 $\mu$g/kg/d (for 10 days) | Antioxidant assay, histopathological assay | ↓ ALT, ↓ LDH, ↓ LPO, ↓ ALP, ↓ acid phosphatase, ↓ urea & ↓ creatinine. ↑ GPx, ↑ GSH, ↑ Catalase & ↑ Vit-C | [7] |
| Aq. leaves extract | Fluoride induced nephrotoxic rats | Sodium Fluoride - 300 & 600 ppm Extract - 500 mg/kg/d (for 20 days) | MDA, GSH, Antioxidant enzymes | ↓ MDA. ↑ GSH, ↑ SOD, ↑ CAT & ↑ GPx | [8] |
| Aq. leaves extract | Gentamicin induced nephrotoxic rats | Gentamicin - 150 mg/kg Extract- 200 & 400 mg/kg/d (for 10 days) | Histopathological identification & estimation of MDA | ↑ Body wt. ↓ BUN, ↓ MDA, ↓ GSH, ↓ Serum creatinine | [10] |
| Ethanolic leaves extract | Cisplatin induced nephrotoxicity | Cisplatin- 5 mg/kg Extract- 200 & 400 mg/kg (for 4 days) | Dot-blot assay, Lipid peroxidation assays | Normalization of urea, creatinine, uric acid, BUN & LPO. ↑ Vit-C | [12] |
| Aq. root extract | Acetaminophen induced nephrotoxic rats | Acetaminophen - 500 mg/kg Extract- 200 & 400 mg/kg/d | Malondialdehyde, Antioxidant enzymes Histopathological studies | ↑ SOD, ↑ CAT, ↑ GSH. ↓ BUN, ↓ MDA, ↓ serum creatinine & ↓ injured cells | [9] |
| Ethanolic root extract | Alloxan induced diabetic nephropathic albino rats | Extract- 500 mg/kg/d (for 30 days) | Blood glucose, insulin assay, serum biochemical assay | Normalised serum $Na^+$, $K^+$& $Na^+$-$K^+$ ATPase activity | [11] |
| Ethanolic root extract | Renal epithelial cell line LLC-PK1 | Cisplastin - (30 $\mu$M) Extract - (250 $\mu$g/ml & 750 $\mu$g/ml) | Accumulation of drug & MTT assay | ↓ No. of apoptotic & ↓ necrotic cells (50%) ↓ ROS production | [15] |

supplied through the diet for 6 months, there was decrease in urine protein and serum creatinine was found to be increased.[14]

Kalaivani and co-workers observed that Cisplatin accumulated in proximal tubular region of kidney had induced toxicity in human. To study for the Nephroprotective activity on renal epithelial cell line LLC-PK1 was used. When cisplatin is treated there was increase in apoptotic and necrotic cells. Again, when the ethanolic root extract is cotreated, there was decrease in number of apoptotic and necrotic cells and attenuation of ROS production is observed. And confirmed that this action is due to presence of phytochemical like, polyphenols, flavonoids and tannins in the extract.[15]

## 2. Conclusion

As the name says Punarnava means once again becoming new, really because of its multiple benefits and pharmacological actions on kidney protection and other beneficial activities it has proved itself as magical natural remedy in Ayurveda. The nephroprotective effect of *Boerhavia diffusa* against Cisplatin induced nephrotoxicity was analysed in Wistar rats by assessing the levels of SOD, CAT, LPO, Vitamin C, TRG, GPx, GR and GST from the kidney of the animals. The plant extract had the ability it to normalize the elevated levels of urea, creatinine, uric acid, BUN in serum and LPO in kidney, also changed the parameters like normalized ion concentration in kidney, improved cell damage when various extract is treated. By all these researches showed that the *Boerhavia diffusa* has protective effect on kidney and from its diseases. Several studies using laboratory animals and very few human studies are available and the studies showed the potential of protective effect on kidney and its toxicity. So, the results obtained may be necessarily be portable to the situation in humans. So further toxicity test on the plant especially during prolonged administration is essential, which need to be bridged. It is very clear that this is a plant with tremendous widespread use now and also with extraordinary potential for the future. So, we can say that it has been proved as a magical drug due to its multidirectional work. Several ayurvedic products are in market with regard to kidney disease as diuretic agents.

## 3. Source of Funding

None.

## 4. Conflict of Interest

None.

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