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EVALUATION OF THE NEPHROPROTECTIVE ACTIVITY OF EXTRACT LEAVES OF ALLIUM CEPA IN SWISS ALBINO MICE WITH GENTAMICIN-INDUCED NEPHROTOXICITY: IN VIVO STUDY

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Article History	Abstract
Received: 19-06-2026 Revised: 24-07-2026 Accepted: 29-08-2026	The present study was undertaken to evaluate the nephroprotective potential of the ethanolic extract of <i>Allium cepa</i> against gentamicin-induced nephrotoxicity in male Wistar rats. Thirty healthy male Wistar rats weighing 150–200 g were randomly divided into five groups of six animals each. Group I served as the normal control, while Group II received gentamicin (80 mg/kg, i.p.) to induce nephrotoxicity. Groups III–V received a standard drug and ethanolic extract of <i>Allium cepa</i> at doses of 200 and 400 mg/kg, respectively, along with gentamicin for 10 days. On day 11, blood samples were collected for biochemical estimation, and the kidneys were excised for histopathological examination. Gentamicin administration resulted in marked renal dysfunction, evidenced by significant increases in blood urea, uric acid, and serum creatinine levels, accompanied by histopathological alterations in the renal tissues. Treatment with <i>Allium cepa</i> extract significantly attenuated these biochemical changes and improved the histological architecture of the kidneys in a dose-dependent manner, with the higher dose showing greater protective activity. The findings demonstrate that the ethanolic extract of <i>Allium cepa</i> possesses promising nephroprotective activity against gentamicin-induced renal injury. Further investigations are required to elucidate the underlying mechanisms and identify the active phytoconstituents responsible for this protective effect.
Keywords: Allium cepa; Nephrotoxicity; Nephroprotective activity; Gentamicin; Wistar rats; Serum creatinine.	
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INTRODUCTION

Kidneys are vital organs responsible for excretion of metabolic wastes and regulation of fluid, electrolyte, acid–base and endocrine functions. Each kidney contains numerous nephrons, the structural and functional units responsible for glomerular filtration, tubular reabsorption and secretion. Because the kidneys receive a high proportion of cardiac output and possess extensive tubular surface area and active transport mechanisms, they are particularly susceptible to toxic injury. Nephrotoxicity may result from drugs, chemicals, heavy metals and other endogenous or exogenous agents and can manifest as acute or chronic renal dysfunction [1-2]. Common nephrotoxic drugs include aminoglycosides, cisplatin, NSAIDs, paracetamol and certain antimicrobial agents. **Gentamicin-induced nephrotoxicity** primarily affects proximal tubular cells. Gentamicin is taken up by tubular epithelial cells through endocytosis and accumulates in lysosomes, where it interacts with membrane phospholipids and inhibits lysosomal phospholipases, resulting in phospholipidosis, cellular injury and tubular necrosis [3-4]. Oxidative stress and free-radical generation further contribute to renal damage. Clinically and experimentally, gentamicin nephrotoxicity is characterized by elevated blood urea and serum creatinine, tubular dysfunction and histopathological alterations [5]. **Cisplatin-induced nephrotoxicity** is another widely used experimental model. Cisplatin accumulates in renal tubular cells, particularly in the proximal tubules, where it induces oxidative stress,

mitochondrial dysfunction, inflammation and apoptosis, leading to tubular injury and impaired renal function. **Paracetamol** can also produce renal injury, particularly following overdose or prolonged exposure, through oxidative stress, glutathione depletion and formation of reactive metabolites, resulting in tubular damage [6-8]. **Diclofenac**, an NSAID, may cause renal injury mainly through inhibition of prostaglandin synthesis, which can reduce renal blood flow and promote ischemic damage. Overall, nephrotoxic injury involves multiple mechanisms, including oxidative stress, mitochondrial dysfunction, altered calcium homeostasis, membrane and lysosomal damage, inflammation and apoptosis. These experimental models are therefore useful for evaluating potential nephroprotective agents and identifying compounds capable of preserving renal biochemical and structural integrity [9-10].

EXPERIMENTAL SECTION

The present study was undertaken to evaluate the *in vivo* nephroprotective activity of the ethanol extract of *Allium cepa* L. against gentamicin-induced nephrotoxicity in rats. The plant material was collected, authenticated, shade-dried, powdered and extracted with ethanol using a Soxhlet apparatus. The concentrated extract was subjected to preliminary phytochemical screening for major classes of phytoconstituents. Adult Wistar albino rats weighing 180–200 g were used following acclimatization under standard

laboratory conditions and ethical approval. Acute oral toxicity was assessed according to standard guidelines, and doses of 200 and 400 mg/kg were selected for the study. Thirty rats were randomly divided into five groups of six animals each. The control group received saline, while nephrotoxicity was induced in the remaining groups using gentamicin (80 mg/kg, i.p.) for 10 days. Treatment groups received *A. cepa* extract at 200 and 400 mg/kg orally, while silymarin (25 mg/kg) served as the standard drug. At the end of the treatment period, blood samples were collected for estimation of blood urea, serum creatinine and uric acid, and kidneys were excised for gross and histopathological examination [12-13]. Blood urea, creatinine and uric acid were estimated using standard biochemical methods, including the GLDH kinetic, modified Jaffe's kinetic and uricase-peroxidase methods, respectively. The results were expressed as mean $\pm$ SEM and analyzed using one-way ANOVA followed by an appropriate post-hoc test, with $p < 0.05$ considered statistically significant.

RESULTS

Gentamicin administration at 80 mg/kg, i.p. for 10 consecutive days produced marked nephrotoxicity in the toxicant control group, as evidenced by significant elevations in serum creatinine and blood urea compared with the normal control group. Serum creatinine increased from 0.680 ± 0.041 mg/dL in the normal control group to 2.214 ± 0.036 mg/dL, while blood urea increased from 21.421 ± 1.205 to 117.63 ± 1.261 mg/dL following Gentamicin administration. Treatment with the ethanolic extract of *Allium cepa* significantly attenuated these elevations in a dose-dependent manner. The 200 mg/kg dose reduced serum creatinine and blood urea to 0.901 ± 0.036 and 54.132 ± 1.125 mg/dL, respectively, whereas the 400 mg/kg dose produced greater reductions to 0.756 ± 0.042 and 49.214 ± 1.362 mg/dL. The standard drug silymarin produced values of 0.712 ± 0.031 and 47.205 ± 1.112 mg/dL, respectively. Serum uric acid showed a comparatively modest increase following Gentamicin administration, from 6.012 ± 0.120 mg/dL in the normal group to 7.212 ± 1.135 mg/dL in the toxicant group. Treatment with *A. cepa* reduced uric acid levels to 5.125 ± 0.126 and 4.625 ± 0.102 mg/dL at 200 and 400 mg/kg, respectively, indicating improvement in renal function (Table 1). Gentamicin administration also increased kidney weight from 0.652 ± 0.014 g in the normal group to 0.725 ± 0.036 g [14-16]. Treatment with *A. cepa* decreased kidney weight to 0.689 ± 0.046 g and 0.562 ± 0.006 g at 200 and 400 mg/kg, respectively, while silymarin produced a value of 0.526 ± 0.006 g (Table 2). These findings suggest that the extract attenuated the renal enlargement associated with Gentamicin-induced injury. Furthermore, Gentamicin significantly elevated serum SGPT, SGOT and ALP levels compared with the normal control. SGPT increased from 44.15 ± 1.60 to 123.12 ± 1.02 U/L, SGOT from 42.25 ± 0.23 to 135.12 ± 1.63 U/L, and ALP from 32.26 ± 1.52 to 94.25 ± 1.74 U/L. Administration of *A. cepa* significantly reduced these enzyme levels in a dose-dependent manner. At 200 mg/kg, SGPT, SGOT and ALP were reduced to 87.20 ± 0.12 , 94.36 ± 1.25 and 76.85 ± 1.18 U/L, respectively, whereas the 400 mg/kg dose produced greater reductions to 65.10 ± 2.21 , 55.20 ± 1.10 and

54.26 ± 2.25 U/L. Silymarin produced values of 45.36 ± 1.12 , 49.14 ± 2.25 and 46.14 ± 0.24 U/L, respectively (Table 3). Histopathological examination supported the biochemical findings. The kidneys of normal control rats showed preserved glomeruli, intact Bowman's capsules and normal proximal and distal convoluted tubules. In contrast, Gentamicin-treated rats exhibited severe renal alterations, including glomerular degeneration and congestion, tubular epithelial damage, tubular lumen obliteration, tubular casts and peritubular congestion, indicating marked tubular injury. Treatment with *A. cepa* at 200 mg/kg resulted in partial restoration of renal architecture, with mild tubular cast deposition and comparatively preserved tubular structures [17-19]. The 400 mg/kg dose showed substantially improved renal morphology, with normal glomeruli and Bowman's capsules and minimal tubular abnormalities. The protective effect observed at 400 mg/kg was comparable to that of the standard treatment. The observed elevation of serum urea and creatinine following Gentamicin administration is consistent with impaired glomerular filtration and renal tubular injury [20-21]. Gentamicin is preferentially accumulated in proximal tubular cells, where it can induce oxidative stress, lysosomal dysfunction, membrane injury and subsequent tubular necrosis. The significant reduction of these renal biomarkers following *A. cepa* treatment suggests that the extract may preserve renal function and reduce Gentamicin-associated tubular damage. The dose-dependent response was particularly evident with the 400 mg/kg dose, which produced values approaching those observed with silymarin [22-24]. The reduction in uric acid, kidney weight and serum enzyme levels further supports the protective effect of the extract. The nephroprotective activity of *A. cepa* may be associated with its flavonoids, polyphenols and other antioxidant phytoconstituents, which may reduce oxidative damage and protect renal cellular structures. Overall, the biochemical and histopathological observations demonstrate that ethanolic extract of *Allium cepa*, particularly at 400 mg/kg, exerted significant protective effects against Gentamicin-induced nephrotoxicity in rats.

Table 01: Effect of Gentamicin and ethanolic extract of *Allium cepa* on serum creatinine, blood urea and uric acid in rats after 10 days

Group	Treatment	Serum Creatinine (mg/dL)	Blood Urea (mg/dL)	Uric Acid (mg/dL)
I	Normal saline	0.680 ± 0.041	21.421 ± 1.205	6.012 ± 0.120
II	Gentamicin 80 mg/kg	2.214 ± 0.036	117.630 ± 1.261	7.212 ± 1.135
III	Gentamicin + <i>A. cepa</i> 200 mg/kg	$0.901 \pm 0.036^{**}$	$54.132 \pm 1.125^{***}$	$5.125 \pm 0.126^{*}$
IV	Gentamicin + <i>A. cepa</i> 400 mg/kg	$0.756 \pm 0.042^{***}$	$49.214 \pm 1.362^{***}$	$4.625 \pm 0.102^{**}$
V	Gentamicin + Silymarin 25 mg/kg	$0.712 \pm 0.031^{***}$	$47.205 \pm 1.112^{***}$	$3.251 \pm 0.122^{**}$

Values are expressed as mean $\pm$ SEM, n = 6. $p < 0.05$, $*p < 0.01$, $**p < 0.001$ versus Gentamicin control.

Table 02: Effect of Gentamicin and ethanolic extract of *Allium cepa* on kidney weight in rats after 10 days

Group	Treatment	Kidney Weight (g)
I	Normal saline	0.652 $\pm$ 0.014
II	Gentamicin 80 mg/kg	0.725 $\pm$ 0.036
III	Gentamicin + <i>A. cepa</i> 200 mg/kg	0.689 $\pm$ 0.046***
IV	Gentamicin + <i>A. cepa</i> 400 mg/kg	0.562 $\pm$ 0.006***
V	Gentamicin + Silymarin 25 mg/kg	0.526 $\pm$ 0.006***

Values are expressed as mean $\pm$ SEM, n = 6. $**p < 0.001$ versus Gentamicin control.

Table 03: Effect of Gentamicin and ethanolic extract of *Allium cepa* on serum SGPT, SGOT and ALP levels in rats after 10 days

Group	Treatment	SGPT (U/L)	SGOT (U/L)	ALP (U/L)
I	Normal saline	44.15 $\pm$ 1.60	42.25 $\pm$ 0.23	32.26 $\pm$ 1.52
II	Gentamicin 80 mg/kg	123.12 $\pm$ 1.02**	135.12 $\pm$ 1.63***	94.25 $\pm$ 1.74***
III	Gentamicin + <i>A. cepa</i> 200 mg/kg	87.20 $\pm$ 0.12**	94.36 $\pm$ 1.25***	76.85 $\pm$ 1.18**
IV	Gentamicin + <i>A. cepa</i> 400 mg/kg	65.10 $\pm$ 2.21***	55.20 $\pm$ 1.10***	54.26 $\pm$ 2.25**
V	Gentamicin + Silymarin 25 mg/kg	45.36 $\pm$ 1.12***	49.14 $\pm$ 2.25***	46.14 $\pm$ 0.24***

Values are expressed as mean $\pm$ SEM, n = 6. $p < 0.05$, $*p < 0.01$, $**p < 0.001$ versus Gentamicin control.

Histopathological observations: The normal control kidney showed normal glomeruli with intact Bowman's capsules and well-preserved proximal and distal convoluted tubules. Gentamicin administration produced severe pathological alterations, including glomerular congestion and degeneration, tubular epithelial damage, tubular casts, peritubular congestion and narrowing or obliteration of tubular lumina. The 200 mg/kg *A. cepa* treatment showed partial protection, with comparatively preserved renal architecture and mild tubular cast formation. The 400 mg/kg treatment showed marked preservation of renal morphology, with normal-looking glomeruli and Bowman's capsules and minimal tubular abnormalities. The silymarin-treated group also demonstrated considerable protection against Gentamicin-induced renal damage. These histological findings were consistent with the biochemical results and further confirmed the nephroprotective potential of *A. cepa*.

CONCLUSION

The present study demonstrated that the ethanolic extract of *Allium cepa* possesses significant nephroprotective activity against Gentamicin-induced nephrotoxicity in rats. Gentamicin

administration produced marked renal injury, as evidenced by increased serum urea, creatinine and uric acid levels, increased kidney weight, alterations in serum SGPT, SGOT and ALP levels, and characteristic histopathological changes including glomerular and peritubular congestion, tubular degeneration and tubular cast formation. Co-administration of *A. cepa* extract significantly attenuated these biochemical and histopathological alterations in a dose-dependent manner, with the 400 mg/kg dose showing greater protection than the 200 mg/kg dose and an effect comparable to the standard drug silymarin. The nephroprotective activity may be associated with the antioxidant potential of phytoconstituents such as flavonoids, phenolics, alkaloids and saponins present in the extract, which may help reduce oxidative damage and preserve renal cellular integrity. Overall, the findings support the potential of ethanolic *A. cepa* extract as a promising natural nephroprotective agent against Gentamicin-induced renal injury. Further studies are required to elucidate its precise molecular mechanisms, identify the active constituents and establish its safety and therapeutic potential.

AUTHOR CONTRIBUTIONS

Both authors contributed to equally.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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