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Research Article

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Nephroprotective Power of *Allium ampeloprasum Subsp. Iranicum*: Attenuating Cyclophosphamide-Induced Kidney Injury through Antioxidant and Anti-Inflammatory Mechanisms

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Abstract

The kidneys are essential organs that perform key functions for maintaining homeostasis. Cyclophosphamide (CP), a widely used chemotherapy agent, can cause nephrotoxicity through multiple mechanisms driven by oxidative stress. *Allium ampeloprasum subsp. Iranicum*, known for its antioxidant and anti-inflammatory properties, contains bioactive compounds that may mitigate these adverse effects. The study aims to determine whether the antioxidant properties of *A. ampeloprasum* can help maintain kidney function and enhance the effectiveness of treatment during CP therapy. Mice were divided into four groups: negative control, *A. ampeloprasum* only (150 mg/kg), CP-treated (20 mg/kg), and combined *A. ampeloprasum* (150 mg/kg) with CP (20 mg/kg). Treatments were administered both orally and intraperitoneally over 14 days. Blood and tissue samples were analyzed for biochemical, histopathological, and molecular markers, including lipid peroxidation, antioxidant enzymes, and inflammatory cytokines. The data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test for multiple comparisons. CP treatment resulted in significant weight loss, tissue inflammation, and structural kidney damage, along with elevated serum markers of kidney injury, increased lipid peroxidation, and decreased antioxidant enzyme activities. Histopathological analysis confirmed inflammatory changes and tissue disruption caused by CP, which were significantly mitigated by pretreatment with *A. ampeloprasum* extract. This extract reduced serum levels of urea, creatinine, and uric acid, and decreased lipid peroxidation in tissues. It boosted antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px). Additionally, *A. ampeloprasum* pretreatment markedly reduced levels of inflammatory cytokines compared with CP alone. This study demonstrates that *A. ampeloprasum* extract effectively mitigates CP-induced toxicity by reducing oxidative stress, inflammation, and tissue damage, indicating its potential as a natural protective agent during chemotherapy.

Keywords: *Allium ampeloprasum subsp. Iranicum*; Kidney Injury; Cyclophosphamide; Nephrotoxicity; Inflammation; Antioxidant.

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1. Introduction

The kidneys are essential organs that perform a wide range of critical functions to maintain homeostasis and overall health. They filter blood, regulate fluid and mineral balance, remove waste products, and help control blood pressure and red blood cell production [1]. Cyclophosphamide (CP) is a widely used alkylating agent in chemotherapy. While it is effective against a broad spectrum of malignancies and autoimmune conditions, it can induce nephrotoxicity through multiple, interrelated mechanisms [2, 3]. The drug's nephrotoxic potential stems from reactive metabolites, notably acrolein, as well as hemodynamic alterations, blood pressure fluctuations, and oxidative stress. The principal pathogenic pathways include direct renal tubular toxicity, changes in renal perfusion, oxidative injury, glomerular involvement, and immune/inflammatory processes. Clinically, CP-associated nephrotoxicity may present as acute kidney injury (AKI), characterized by reduced urine output and elevated serum creatinine, along with proteinuria or hematuria and disturbances in electrolyte balance. Repeated or chronic exposure carries a risk of progression to chronic kidney disease (CKD) [4, 5]. Although the exact mechanisms are not fully understood, oxidative stress is considered a key pathway contributing to drug-induced nephrotoxicity. Oxidative stress arises when excessive reactive oxygen species (ROS) overwhelm the body's antioxidant defences, leading to cellular damage. During CP metabolism and the breakdown of its metabolites, ROS such as superoxide anions, hydroxyl radicals, and hydrogen peroxide are generated. This radical production can disrupt multiple signalling pathways, including inflammatory cascades, and may contribute to organ fibrosis over time [4, 6].

Plant-derived antioxidants offer a promising strategy to counteract CP-induced nephrotoxicity by mitigating oxidative stress, modulating inflammatory and fibrotic pathways, and preserving renal function. Evidence from preclinical models suggests that polyphenols, flavonoids, and other phytochemicals can ameliorate oxidative damage and improve renal outcomes following nephrotoxic insults [4, 7].

Allium ampeloprasum subsp. Iranicum (*A. ampeloprasum*), a regional variant of the genus *Allium* in the Amaryllidaceae family, offers a rational and locally feasible candidate for nephroprotection due to its rich phytochemical profile, including organosulfur compounds, polyphenols, and flavonoids [8]. These constituents underpin antioxidant, anti-inflammatory, and anti-fibrotic properties that align with the mechanistic pathways of CP-induced kidney injury, such as oxidative stress, nuclear factor kappa beta (NF-κB)/TNF-α signalling, and apoptosis, suggesting potential to mitigate ROS overproduction, lipid peroxidation, and inflammatory cascades while preserving renal tubular integrity and reducing fibrotic progression [7]. Ethnopharmacological use and dietary familiarity further support its feasibility, though rigorous toxicity and interaction assessments are essential in the context of chemotherapy [9, 10]. Key therapeutic actions to be investigated encompass scavenging of reactive oxygen species, upregulation of endogenous antioxidant defenses, inhibition of proinflammatory mediators, and attenuation of renal cellular injury; The study aimed to test specific hypotheses: 1) *A. ampeloprasum* extract reduces CP-induced renal dysfunction (lower serum urea, creatinine, uric acid); 2) It attenuates oxidative stress by decreasing lipid peroxidation (MDA) and restoring antioxidant enzymes; 3) It exerts anti-inflammatory effects by lowering proinflammatory cytokines; and 4) These effects correlate with improved kidney histology. The experimental design was structured to first profile the extract's phytochemistry and then evaluate these parameters in a CP-treated mouse model.

2. Materials and Methods

2.1. A. ampeloprasum extract preparation

In spring 2023, *A. ampeloprasum subsp. Iranicum* was gathered from the Chaharmahal and Bakhtiari Mountains of Iran. The specimen received exact identification by a group of expert botanists from the Islamic and Complementary Medicine Department, Iran University of Medical Sciences, Tehran, Iran. A 100 g sample of the dried whole plant powder was extracted by maceration in 300 mL of an 80:20 ethanol–water solvent. The extract was concentrated using a rotary evaporator, then freeze-dried, and finally dried in a vacuum oven at 40°C for 5 days. The resulting material was stored at 4°C until use. The Folin–Ciocalteu spectrophotometric method was

used to determine total phenolic content, with gallic acid as the standard, and total flavonoid content was measured by a colorimetric assay using quercetin as the standard [11].

2.2. Animals

Six- to eight-week-old NMRI mice (male), weighing 28–32 g, were obtained from the Faculty of Medical Sciences at Tarbiat Modares University, Tehran, Iran. Before experimentation, the mice were housed in polystyrene cages (five per cage) and acclimatized to the laboratory conditions for one week. Throughout acclimation, they were maintained at 20–22°C, with a relative humidity of about 35%, and a 12-hour light/dark cycle, with ad libitum access to standard rodent chow and drinking water [2]. All procedures complied with ethical standards and were approved by the Ethical Committee of Tarbiat Modares University (Approval No. IR.MODARES.AEC.1401.014).

2.3. Treatment protocols

NMRI mice were randomly divided into four groups, each with five animals:

Group 1: Received an oral dose of 150 mg/kg of *A. ampeloprasum* extract daily for 14 consecutive days.

Group 2: Received an oral dose of 150 mg/kg of *A. ampeloprasum* extract daily for 14 days, with intraperitoneal (IP) injections of CP at 20 mg/kg during the last 5 days.

Group 3 (Positive control): Received IP injections of CP at 20 mg/kg for five days.

Group 4 (Negative control): Received normal saline orally for 14 days.

Protocols are based on prior studies [8].

2.4. Body and relative organ weight

To assess weight alterations, the body mass of each mouse was recorded at baseline (day 1) before the initial treatment. On day 14, two hours after the final dose administration, the animals were anesthetized with ketamine (100 mg/kg) and xylazine (10 mg/kg). After anesthesia, the mice were euthanized by severing the spinal cord. The kidney weight was measured manually, and relative organ weights were determined as the ratio of organ mass to total body mass [2].

2.5. Serum collection and tissue preparation

Before tissue collection, each mouse underwent individual blood collection via cardiac puncture, with the samples deposited into sterile, dry centrifuge tubes. The samples were allowed to coagulate at 37°C for 10 minutes, after which they were centrifuged at 2,500 rpm for 10 minutes to separate the serum. The serum was dispatched to a laboratory for biochemical analysis to assess a broad range of parameters. In the next step, the kidneys were carefully dissected and rinsed with ice-cold isotonic saline to remove blood and debris. Tissues designated for histopathological evaluation, lipid peroxidation, and antioxidant enzyme assays were prepared accordingly.

2.6. Histopathological studies

For histopathology, kidney tissue was fixed in 10% neutral-buffered formalin for 24–48 hours. After fixation, the samples were processed, embedded in paraffin, and sectioned into 5 µm thick slices. The sections were stained with hematoxylin and eosin (H&E) and examined under a light microscope to assess morphological changes indicative of tissue injury or pathology [12].

2.7. Biochemical parameters

Kidney function was assessed by measuring serum creatinine and urea levels [13].

2.8. Lipid peroxidation assay

MDA levels, a marker of lipid peroxidation, were quantified using the thiobarbituric acid (TBA) assay kit (NalondiTM Lipid Peroxidation (MDA) Assay Kit, Navand Salamat, Iran) according to the manufacturer's instructions [14].

2.9. Antioxidant enzymes assay

Antioxidant enzyme activities in kidney tissue were measured using commercial assay kits. Specifically, superoxide dismutase (SOD) was assessed with the Nasdox™ SOD Assay Kit (Navand Salamat, Iran), catalase (CAT) activity was determined with the Nactaz™ Catalase Enzyme Activity Assay Kit (Navand Salamat, Iran), and glutathione peroxidase (GSH-Px) activity was

evaluated using the Glutathione Peroxidase Assay Kit (Navand Salamat, Iran). All assays were performed according to the manufacturer's protocols [12].

2.10. Inflammatory cytokine parameters

Kidney inflammatory cytokines, including interleukin-6 (IL-6) (CN: KPG-MIL6, Karmania Pars Gene, Iran), interleukin-1β (IL-1β) (CN: KPG-MIL1b, Karmania Pars Gene, Iran), and tumor necrosis factor-α (TNF-α) (CN: KPG-MTNF-a, Karmania Pars Gene, Iran), were measured using commercial enzyme-linked immunosorbent assay (ELISA) kits in accordance with the manufacturers' protocols [15].

2.11. Statistical analyses

All data are expressed as mean ± standard deviation (SD). The data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test for multiple comparisons. A p-value of less than 0.05 was considered statistically significant. All analyses were performed using Prism version 10.

3. Results and Discussion

3.1. Total flavonoid and phenolic compounds content

Each gram of the dry extract contained 197.85 mg of total phenolics and 334/66 mg of total flavonoids.

3.2. Body and relative kidney weight

Baseline body weights did not differ significantly among experimental groups. After treatment, the *A. ampeloprasum* group showed a statistically significant increase in body weight compared with the negative control group ($p < 0.001$). Conversely, the CP group showed a significant reduction in body weight compared with the negative control group ($p < 0.05$).

Analysis of kidney weight showed no significant difference between the negative control and *A. ampeloprasum* groups. However, CP administration resulted in a significant reduction in kidney weight compared to the negative control group ($p < 0.01$). The relative kidney weight also did not differ significantly between the negative control group and the *A. ampeloprasum* groups. Notably, the CP-treated group had a significant reduction in relative kidney weight compared to the negative control group ($p < 0.01$) (**Table 1**).

3.3. Histopathological study

As shown in **Figure 1**, histopathological examination of the kidneys showed that the negative control group and the group treated with *A. ampeloprasum* extract alone showed normal renal tissue architecture. In contrast, the group treated with CP showed significant renal tissue damage and obvious morphological abnormalities such as extensive vacuolation of cells with significant hypertrophy, as well as disruption of renal structure. In addition, mild leukocyte infiltration was observed (**Figure 1C**). Pretreatment with *A. ampeloprasum* extract before CP administration resulted in significant restoration of normal renal morphology and structure and a significant reduction of vacuolation (**Figure 1D**).

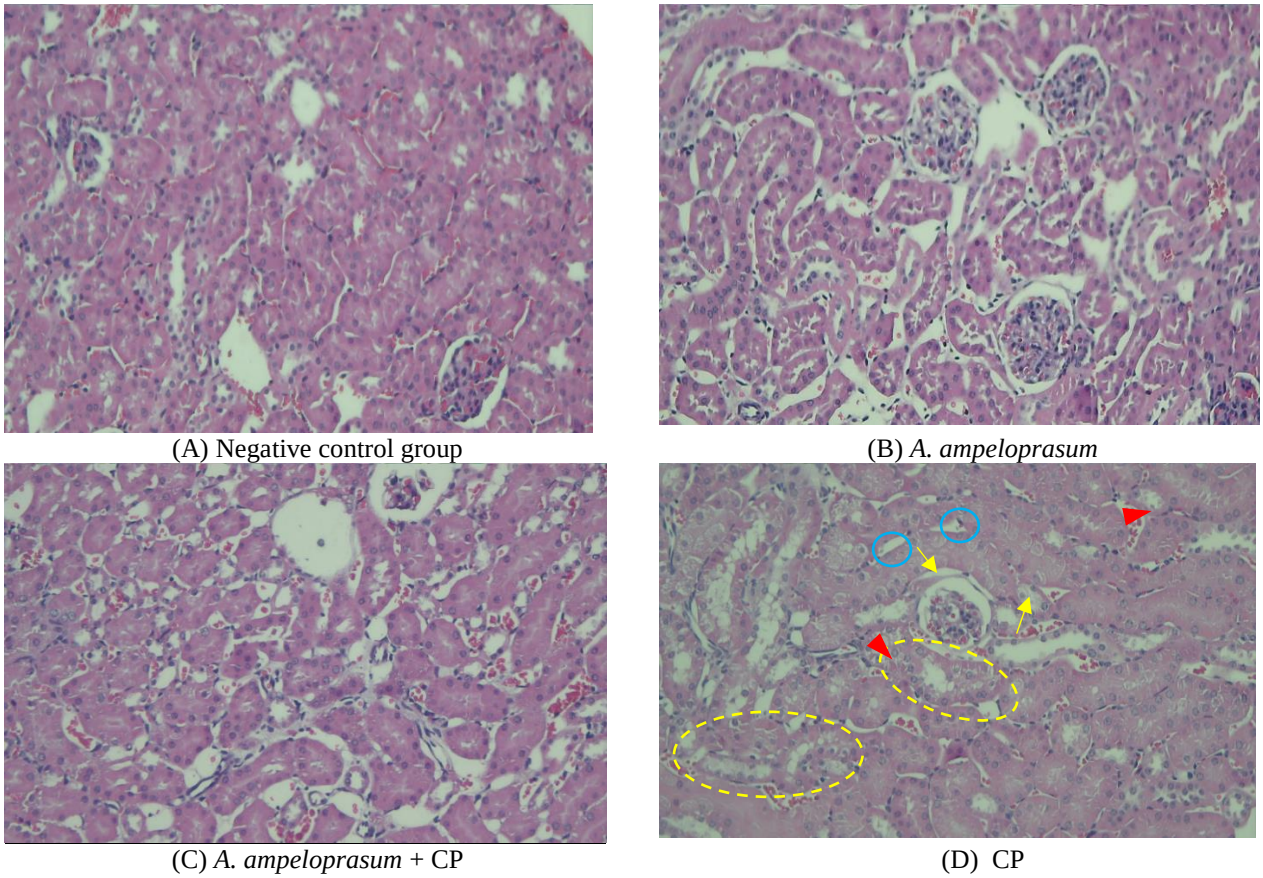
3.4. Biochemical parameters

As indicated in Table 2, renal toxicity was observed following CP intraperitoneal injection, characterized by a notable increase in serum levels of urea, creatinine, and uric acid ($p < 0.001$) compared to the negative control group. In this context, pretreatment with *A. ampeloprasum* significantly decreased the serum levels of urea, creatinine, and uric acid ($p < 0.01$, $p < 0.05$, $p < 0.01$, respectively).

Table 1. The protective effect of *A. ampeloprasum* on body weight and kidney weight in mice.

Parameter	Negative control	*A. ampeloprasum*	*A. ampeloprasum* + CP	CP
Body weight (g) Before	28.2±3.1	31.2±2.15	31.36±3.9	28.8±4.8
Body weight (g) After	33.4±3.3.5	36.8±1.5***	34±2.9##	29.6±2.2*
Kidney weight (mg)	304 ± 5.1	328 ± 4.3	315 ± 3.5##	270** ± 2.3
Relative body weight (%BW)	0.91%	0.89%	0.92%	0.91%

The data are presented as mean ± SD (n = 5)
* $p < 0.05$, **$p<0.01$, and ***$p<0.001$ indicate significant changes compared to the control group.
##$p<0.01$ indicates significant changes compared to the CP group.
CP: Cyclophosphamide, %BW: body weight percentage.



(A) Negative control group (B) *A. ampeloprasum*

(C) *A. ampeloprasum* + CP (D) CP

Figure 1. The impact of *A. A. ampeloprasum* on the kidney tissue histopathology. Representative pictures of kidney tissue stained with hematoxylin and eosin (H&E) examined under a microscope (magnification: ×200). CP: Cyclophosphamide. Yellow arrows indicate vacuolization of cells, and yellow dashed circles indicate notable morphological disintegration of the renal architecture. Blue encircles hypertrophic cells with significant, obvious vacuolization. Red arrowheads display mild infiltration of inflammatory leukocytes.

3.5. Lipid peroxidation assay

As shown in **Figure 2**, CP intraperitoneal injection resulted in a significant increase in kidney TBARS levels compared with the negative control group ($p < 0.001$). However, pretreatment with *A. ampeloprasum extract* reduced TBARS levels in the treated group ($P < 0.001$).

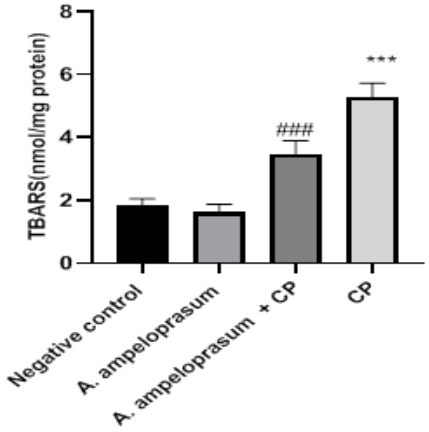


Figure 2. The effect of *A. ampeloprasum* on the kidney lipid peroxidation. Data are presented as mean ± standard deviation (n = 5). Statistical analyses were conducted by the Tukey-Kramer test; ***p < 0.001 shows significant differences relative to the normal saline group. Furthermore, p < 0.001 indicates a significant difference compared to the CP group. CP: Cyclophosphamide, TBARS: Thiobarbituric acid reactive substances.

3.6. Antioxidant enzymes assessments

3.6.1. SOD activity

Figure 3 shows that SOD activity was markedly decreased in kidney tissue from the CP group compared to the negative group ($p < 0.001$). In contrast, administration of *A. ampeloprasum* significantly increased SOD activity in kidney tissue ($p < 0.05$).

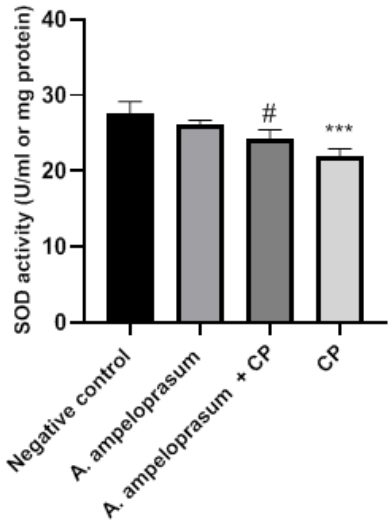


Figure 3. The effect of *A. ampeloprasum* on the kidney tissues' SOD activity. Data are presented as mean ± standard deviation (n = 5). Statistical analyses were conducted by the Tukey-Kramer test; ***p < 0.001 shows significant differences relative to the normal saline group. Furthermore, #P < 0.05 indicates a significant difference compared with the CP group. CP: Cyclophosphamide; SOD: superoxide dismutase.

3.6.2. CAT activity

The results shown in **Figure 4** demonstrate that CAT activity in kidney tissue was significantly reduced in the CP group compared with the negative group (p < 0.001). Conversely, treatment with *A. ampeloprasum* extract markedly elevated CAT activity in this tissue (p < 0.01).

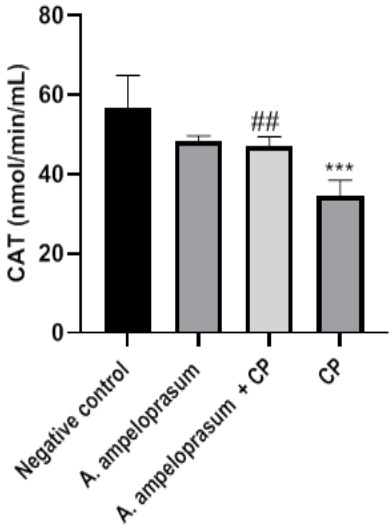


Figure 4. The effect of *A. ampeloprasum* on the kidney tissue's CAT activity. Data are presented as mean ± standard deviation (n = 5). Statistical analyses were conducted by the Tukey-Kramer test; ***p < 0.001 shows significant differences relative to the normal saline group. Furthermore, ##P < 0.01 signifies a significant difference when compared to the CP group. CAT: Catalase; CP: Cyclophosphamide.

3.6.3. GSH-Px activity

The data in **Figure 5** indicate that GSH-Px activity was significantly lower in kidney tissue from the CP group than in the negative control group (p < 0.001). Conversely, administration of *A. ampeloprasum* resulted in a significant restoration of GSH-Px activity, markedly increasing the enzyme activity in this tissue (p < 0.05).

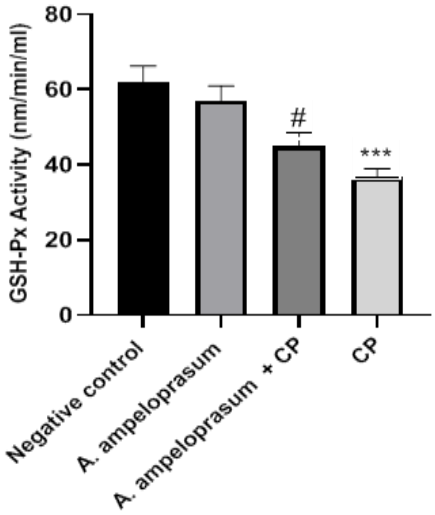


Figure 5. The effect of *A. ampeloprasum* on the kidney GSH-Px activity. Data are presented as mean ± standard deviation (n = 5). Statistical analyses were conducted by the Tukey-Kramer test; ***p < 0.001 shows significant differences relative to the normal saline group. Furthermore, ##p < 0.01 signifies a significant difference when compared to the CP group. CP: Cyclophosphamide, GSH-Px: Glutathione peroxidase.

3.7. Inflammatory cytokine parameters

3.7.1. IL-6

As shown in **Figure 6**, administration of CP results in a notable increase in TNF-α levels in kidney tissue (p < 0.001, respectively). Conversely, administration of *A. ampeloprasum* significantly reduces TNF-α levels in the tissue compared with the CP-only group (p < 0.001).

3.7.2. IL-1β

As shown in **Figure 7**, administration of CP results in a substantial increase in kidney IL-1β levels (p < 0.001). In contrast, pretreatment with *A. ampeloprasum* markedly reduces IL-1β levels compared to the CP-only group in this tissue (p < 0.001).

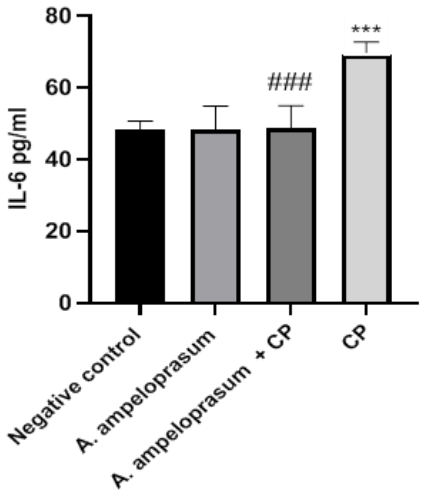


Figure 6. The effect of *A. ampeloprasum* on the kidney level of IL-6. Data are presented as mean ± standard deviation (n=5). Statistical analyses were conducted by the Tukey-Kramer test; ***p<0.001 shows significant differences relative to the normal saline group. Furthermore, p<0.001 indicates a significant difference compared to the CP group. CP: Cyclophosphamide, IL-6: Interleukin 6.

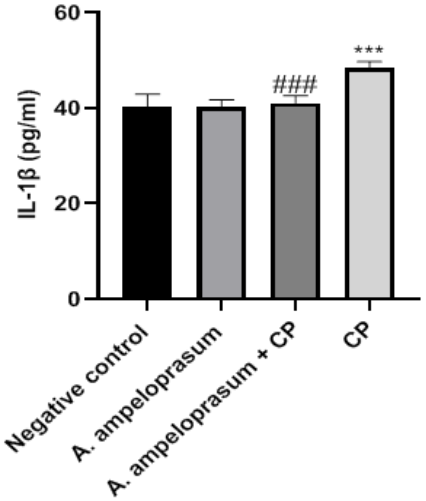


Figure 7. The effect of *A. ampeloprasum* on the level of IL-1β in the kidney. Data are presented as mean ± standard deviation (n = 5). Statistical analyses were conducted by the Tukey-Kramer test; ***p < 0.001 shows significant differences relative to the normal saline group. CP: Cyclophosphamide, Interleukin 1 beta: IL-1β.

3.7.3. TNF-α

The CP group exhibits a significant elevation in TNF-α levels ($p < 0.001$) compared to the negative control group. The pretreatment with *A. ampeloprasum* significantly modulates TNF-α levels compared to the CP group ($p < 0.001$) (**Figure 8**).

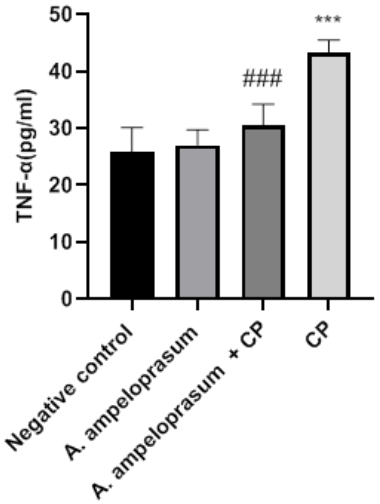


Figure 8. The effect of *A. ampeloprasum* on the level of TNF-α in the kidney tissue. Data are presented as mean ± standard deviation (n = 5). Statistical analyses were conducted by the Tukey-Kramer test; *p < 0.05 and **p < 0.01 show significant differences relative to the normal saline group. Furthermore, p < 0.001 indicates a significant difference compared to the CP group. CP: Cyclophosphamide, TNF-α: Tumor necrosis factor alpha.

3.8. Discussion

The protective potential of *A. ampeloprasum* against CP-induced nephrotoxicity appears to be mediated through a combination of antioxidant, anti-inflammatory, and mitochondrial-protective mechanisms. CP exposure induced renal injury, evidenced by histopathological damage, elevated renal injury biomarkers (urea, creatinine, uric acid), increased lipid peroxidation (TBARS), and suppression of endogenous antioxidant defences (SOD, CAT, GSH-Px), indicating that oxidative stress is a central driver of CP nephrotoxicity. Pretreatment with *A. ampeloprasum* extract significantly mitigated these deleterious effects by improving renal morphology, reducing TBARS, and restoring antioxidant enzyme activities, which suggests that phytochemicals such as phenolics and flavonoids within the extract can directly scavenge ROS/RNS and may upregulate endogenous antioxidant responses, potentially via activation of the nuclear factor erythroid 2–related factor 2 (Nrf2), antioxidant response elements (AREs) pathway leading to increased transcription of antioxidant genes [16]. Moreover, CP-driven increases in proinflammatory cytokines TNF-α and IL-1β were substantially attenuated by the extract, suggesting interference with inflammatory signalling, likely through inhibition of NF-

κB activation and downstream mitogen-activated protein kinase (MAPK) cascades, thereby reducing transcription of proinflammatory mediators and limiting inflammatory cell recruitment to renal tissue [17]. This anti-inflammatory effect complements the antioxidant action, collectively preserving mitochondrial integrity and cellular homeostasis, as suggested by restored SOD, CAT, and GSH-Px activities and reduced lipid peroxidation, thereby mitigating CP-induced mitochondrial dysfunction and apoptosis-related pathways [18]. The observed improvements in renal function markers, histology, and oxidative/inflammatory profiles align with a comprehensive nephroprotective model in which *A. ampeloprasum* acts at multiple nodes of CP-induced nephrotoxicity, including ROS scavenging, enhancement of endogenous antioxidant defences, and suppression of proinflammatory signalling. Future work should delineate the precise molecular mediators, such as Nrf2 nuclear translocation, HO-1/NQO1 expression, IκB-α degradation, and MAPK phosphorylation status, and evaluate the pharmacokinetics and safety of the extract to establish translational relevance.

Several studies on *Allium* species (e.g., *Allium cepa*, *Allium sativum*) report similar nephroprotective effects against cisplatin- or CP-induced toxicity, characterized by upregulation of endogenous antioxidants (SOD, CAT, GPx) and reduction of lipid peroxidation, suppression of proinflammatory cytokines (TNF-α, IL-1β), and attenuation of NF-κB signalling [19-21]. Comparable mechanisms have been observed with other phenolic- and flavonoid-rich plant extracts (e.g., caffeic acid derivatives, quercetin-rich fractions) that activate the Nrf2–ARE axis and inhibit NF-κB/MAPK pathways, resulting in reduced renal injury biomarkers and improved histology [22, 23]. Mitochondrial protection is a recurrent theme; studies using plant extracts with high antioxidant capacity often report preservation of mitochondrial membrane potential, decreased cytochrome c release, and lower caspase activation in nephrotoxic models. The concept of a multitarget protective strategy, scavenging ROS, boosting endogenous defences, and tempering inflammatory signalling, aligns with the polyphenolic nature of *Allium* extracts, which contain diverse bioactives capable of modulating multiple cellular pathways simultaneously [24, 25].

Our findings suggest that the nephroprotective effects of *A. ampeloprasum* extract are mediated through specific biochemical interactions of its phytochemical constituents. The flavonoids and phenolic compounds likely inhibit NF-κB signalling by preventing IκB-α degradation and subsequent nuclear translocation, thereby reducing the transcription of proinflammatory cytokines such as TNF-α and IL-1β. Concurrently, these compounds may activate the Nrf2 pathway by altering Keap1, thereby increasing the expression of antioxidant enzymes, including SOD, CAT, and GSH-Px. Additionally, key flavonoids, such as quercetin, are known to suppress MAPK pathways by inhibiting p38 and JNK phosphorylation, thereby further attenuating inflammatory and oxidative cascades. Together, these multitarget interactions result in reduced oxidative stress, diminished inflammation, and preserved renal structure and function following cyclophosphamide exposure [26, 27].

The magnitude of protection observed with *A. ampeloprasum* may reflect a unique phytochemical profile enriched in specific phenolics and flavonoids that efficiently activate Nrf2 while also inhibiting NF-κB more robustly than some other *Allium* species reported in the literature. Differences in extraction methods, dose, and pretreatment timing across studies can influence the extent of nephroprotection. Standardization of extract composition (e.g., total phenolic and flavonoid contents, identified active constituents) would improve cross-study comparisons [27, 28].

This multimodal action suggests *A. ampeloprasum* could serve as an adjuvant to CP chemotherapy, potentially enabling safer dosing. While direct clinical evidence for this specific extract is not yet available, human trials on other plant antioxidants, such as N-acetylcysteine (NAC) and curcumin, have demonstrated reduced chemotherapy-induced nephrotoxicity in patients, supporting the translational potential of our findings. Future research should focus on isolating the active constituents, establishing clinical pharmacokinetics, and conducting randomized controlled trials to validate its efficacy and safety in human subjects [29-31].

Limitations and Translational Considerations

While the present study demonstrates compelling nephroprotective effects in a murine model, several limitations must be acknowledged before clinical translation can be considered. First, the phytochemical composition of *A. ampeloprasum* extract can vary significantly depending on geographical origin, harvest time, and extraction methodology, necessitating rigorous standardization to ensure consistent efficacy and safety. Second, potential herb-drug interactions, particularly with cyclophosphamide metabolism via cytochrome P450 enzymes, remain unknown and require detailed pharmacokinetic and pharmacodynamic investigation. Third, although no acute toxicity was observed in this short-term study, comprehensive subchronic and chronic toxicity profiles are essential. Future studies should focus on dose optimization, identification of the precise active constituents, and evaluation in higher-order animal models to better predict human response.

4. Conclusion

A. ampeloprasum extract provides strong nephroprotection against CP-induced nephrotoxicity by reducing oxidative stress and enhancing endogenous antioxidant defenses, and it also exerts anti-inflammatory effects, likely via NF-κB/MAPK inhibition, contributing to preserved mitochondrial integrity and renal homeostasis; these findings support a multitarget mechanism and the potential use of *Allium*-derived compounds as a chemotherapy adjuvant, with future work needed on molecular mediators, pharmacokinetics, and standardization.

Conflict of interest

No potential conflict of interest and funding was reported by the author(s).

Authors Contributions

Study concept and design, Critical revision of the manuscript for important intellectual content; Statistical analysis K.SH; Analysis and interpretation of the data: B.Y. and F.A.

Using artificial intelligence chatbots

There was no use of artificial intelligence in the making of this article.

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