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Protective Effect of Alcoholic Extract and Nanoparticles Extract of Prickly Pear Fruit against Thioacetamide-Induced Nephrotoxicity

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Annotation: Objective: this study was to evaluate the preventive impacts of alcoholic and nano extracts of cactus pear fruit (Opuntia ficus-indica) pulp and peel against thioacetamide (TAA)-induced renal toxicity and tissue damage in male albino rats.

Methods: The study involved rats divided into six groups, each with six animals. The first group was given 0.9% NaCl alone for 14 weeks, while the second group received 200 mg/kg of thioacetamide (TAA) diluted in distilled water to induce renal toxicity. The third group received an alcoholic extract of prickly pear (pulp) at 100 mg/kg, followed by TAA administration. The fourth group received an alcoholic extract of prickly pear (peels) at 100 g/kg, followed by TAA administration. The fifth group received a nano-form extract (pulp) at 54 mg/kg, followed by TAA. The sixth group received a nano-form extract (peels) at 50 mg/kg followed by TAA till the conclusion of the study.

Results: TAA exposure markedly raised renal function creatinine and urea and reduced the level of albumin and glomerular atrophy, widened Bowman's space, caused destruction of renal tubule walls, detachment of their epithelial lining, congestion of blood vessels between renal

tubules, destruction of renal tubule walls, and cellular necrosis. Treatment with alcoholic and nano extracts markedly decreased creatinine and urea levels and increased in the level of albumin and improvement in kidney tissue.

Conclusion: These findings suggest that prickly pear fruit extracts demonstrate significant renal protective effects, potentially hindering the advancement of TAA-induced nephrotoxicity.

Keywords: cactus pear; Thioacetamide; nephrotoxicity; nanotechnology; renal damage.

1. Introduction

The kidneys are vital organs that regulate body functions, including erythrocyte production, Calcium-phosphorus homeostasis and pH balance. Chronic kidney disease (CKD) is a condition involving renal inflammation and structural injury [1]. The acronym "CKD" denotes various diseases that impact nephritic structure and function. A variety of ecological and clinical factors may predispose an individual to chronic kidney disease (CKD). Given that chronic kidney disease (CKD) is a worsening global concern, there is an increasing demand for novel preventive therapies that effectively address various forms of renal injury.[2] The kidneys exhibit heightened sensitivity to lipid peroxidation and oxidative stress due to their abundance of long-chain polyunsaturated fatty acids and their role in filtering substantial quantities of pollutants that may accumulate in renal tissues [3]. The kidney's reactions to toxicants exhibited various morphological patterns, ranging from tubular or interstitial alterations to nephropathy [4]. Diverse pathways contribute to renal toxicity, including inflammation, renal tubular toxicity, and glomerular injury [5]. The proximal convoluted renal tubules are essential for the excretion of waste materials from the circulatory system. Their secretory and reabsorptive functions, along with their biotransformation ability, render them particularly susceptible to chemically produced toxicity and ensuing renal damage. Thioacetamide (TAA) is an established industrial agent used in a variety of laboratory and manufacturing settings, including metallurgy, fungicide production, pesticide formulation. in hepatic biotransformation by cytochrome P450 enzymes, TAA is first converted to thioacetamide S-oxide, which is then oxidized to thioacetamide S,S-dioxide, a highly reactive intermediate involved in cell necrosis [7].

The production of reactive oxygen species (ROS) is augmented by TASO2, which enhances the generation of significantly increasing the production of peroxide radicals. As a result, oxidative stress increases, accelerating processes such as lipid peroxidation. The kidneys are main locations for the accumulation of these metabolites [8]. Exposure to TAA results in considerable renal dysfunction, as seen by elevated serum levels of uric acid, blood urea nitrogen (BUN), creatinine, and notable histological changes [9].

Natural products have garnered increasing attention for their potential to counteract the toxic effects of chemical agents due to their abundance of bioactive compounds with antioxidative and anti-inflammatory properties [10]. The cactus pear (*Opuntia ficus-indica* (L.) Miller) is a member of the Cactaceae family. The *Opuntia ficus-indica* serves as a significant source of nutrients and sustenance due to its inherent antioxidants, which may offer protection against oxidative damage [12]. Prickly pear fruits include phytochemical substances such as vitamins, carotenoids, betalains, and polyphenolic chemicals. These compounds have diverse biological actions, including anti-cancer, anti-diabetic, anti-inflammatory, and neuroprotective properties [13]. Consequently, these qualities have rendered Prickly pear fruits increasingly significant in

recent years [14].

2. Materials and methods

2.1 Animals

Thirty-six adults male Wistar albino rats, weighing among 180–250 g, were obtained from the Animal House of the Faculty of Pharmacy, University of Karbala. The animals were housed in spacious polypropylene cages, with six rats per cage. They were allowed a two-week acclimatization period under controlled environmental conditions: temperature in the laboratory ranged from 20 to 23 degrees Celsius, the humidity ranged from 55 to 65%, and a 12-hour light/dark cycle. Animals had full access to food and water.

2.2 Preparation of Plant Extracts

Fresh prickly pear fruit was obtained from a store in Karbala. The fruit was peeled, the pulp was extracted from the peel, and thereafter allowed to desiccate at ambient temperature for sixty days. Subsequent to drying out, the pulp and skin were pulverized to get a finely ground substance.

Alcoholic extract: The alcoholic extract was obtained by combining 50 g of dry powder with 250 ml of ethanol and extracting it via a Soxhlet apparatus for 24 hours, in accordance with the method described in [15]. The extract was subsequently concentrated using a rotary evaporator to produce a dry extract, which was then given orally to the animal at a dosage of 100 mg/kg after being mixed with distilled water.

Nanoparticle extraction: The nano-extract was prepared according to the method of [16] The nanoparticle extraction process involved combining zinc oxide with distilled deionized water and prickly pear extract. The mixture was stirred for 24 hours, then transferred to a shaking incubator for 18 hours. The pH was adjusted to 12 by adding NaOH solution. A nano zinc oxide precipitate was generated, which was isolated, washed, dried, and calcined. The ZnO nanoparticles were pulverized to create a fine powder, which was stored in the refrigerator. Three methods were used to confirm the biosynthesis of nano zinc oxide using prickly pear fruit: nanomolecular atomic force microscopy (AFM), infrared spectroscopy (FTIR), and scanning electron microscopy (SEM).

2.3 Induction of nephrotoxicity

Induction of renal toxicity using Thioacetamide: the nephrotoxicity was induced in rats utilizing thioacetamide (TAA) at a concentration of 200 mg/kg, which was injected by subcutaneous injection twice weekly for 14 weeks.

2.4 Experimentation Design:

The animal was randomly allocated into six experimental groups (n = 6 per group) for a duration of 14 weeks as follows:

- **Group I:** Control group received NaCl (0.9 %). for 14 weeks.
- **Group II:** TAA-treated group received TAA (200 mg/kg, IP) for 14 weeks to induce renal toxicity.
- **Group III:** Received alcoholic extract of prickly pear pulp (100 mg/kg) + TAA (200 g/kg, IP). until the end of the 14-week period.
- **Group IV:** Received alcoholic extract of prickly pear peels (100 mg/kg, IP) + TAA(200 g/kg, IP) until the end of the 14-week period.
- **Group V:** Received nano-form alcoholic extract of prickly pear pulp (54 mg/kg, IP) + TAA (200 g/kg, IP) until the end of the 14-week period.

- **Group VI:** Received nano-form alcoholic extract of prickly pear peels (50 mg/kg, IP) + TAA (200 g/kg, IP) until the end of the 14-week period.

2.5 Sample Collection and Analysis

Blood samples were collected by cardiac puncture and examined to evaluate Renal Function Tests: urea, creatinine in Serum and albumin and some apoptosis and tumor proliferation parameters.

2.6 Histopathological Examination:

Kidney tissue was preserved in 10% formalin, dehydrated through a sequential series of alcohol concentrations, cleared with xylene, and wrapped in paraffin wax. For histological analysis, 5 µm sections were prepared and stained with haematoxylin and eosin.

2.7 Statistical Analysis

Data was analyzed utilizing SPSS software and one-way ANOVA. succeeded by a least significant difference (LSD) test to assess intergroup differences at a significance level ($P<0.05$).

3. Results

3.1 The impact of thioacetamide, Alcoholic Extract, and Nano-Extracts of Prickly Pear Fruit on Kidney Function and albumin.

The results in Table (3-1) showed a significant increase ($P<0.05$) in creatinine and urea levels in the positive control group (G2), which induced nephrotoxicity, compared to the negative control group (G1), which was not exposed to any treatment. Meanwhile, there was a substantial reduction ($P<0.05$) in creatinine and urea concentrations in all groups administered with the alcoholic and nano-extracts in contrast to the infected group (G2). The results demonstrated no statistically variations. ($P>0.05$) among the collections G4 and G3, as well as between groups G5 and G6. However, there were substantial differences ($P<0.05$) among groups G4, G3, and G5, and G6.

The results of Table (3-1) showed a significant decrease ($P<0.05$) in the level of albumin in the positive control group G2, in which nephrotoxicity was induced, compared to the negative control group G1 which was not exposed to any treatment. While there was a substantial elevation ($P<0.05$) in the levels of albumin in all collections treated with alcoholic and nano extracts in comparison to the positive control collection G2. The findings demonstrated no statistically distinctions ($P>0.05$) across the groups. G4, G3, and also between groups G6, G5, but there were notable differences ($P<0.05$) between (G4, G3) and (G6, G5).

Table (3-1) The impact of alcoholic and nanoparticle extracts of cactus pear fruit on Kidney Function and albumin in the blood of male albino rats administered Thioacetamide.

group	S.E ± Means		
	Creatinine µmol/l	Urea (mmol/L 1	Albumin (g/dl)
G1 Negative control group	37.83± 1.04 B	5.46± 0.17 D	5.75± 0.38 A
G2 Positive control (200 mg/kg TAA)	81.00± 3.34 A	9.46± 0.26 A	2.58± 0.18 B
G3 Alcoholic extract group (pulp) (100 mg/kg) + (200 mg/kg TAA)	50.66± 2.77 C	6.33± 0.19 B	4.03± 0.24 C
G4	49.50± 1.96	6.05± 0.18	4.28± 0.19

Alcoholic extract group (peel) (100 mg/kg) + (200 mg/kg TAA)	C	BC	C
G5 Nano-extract group (pulp) (54 mg/kg) + (200 mg/kg TAA)	42.16± 1.01 DB	5.95± 0.17 CBD	5.36± 0.35 DA
G6 Nano-extract group (peel) (50 mg/kg) + (200 mg/kg TAA)	41.66± 1.40 DB	5.68± 0.08 CD	5.63± 0.26 DA
L.S. D	**6.111**	**0.5411**	**0.8121**

Mean ± standard error n = 6

Different capital letters in vertical direction demonstrate substantial disparities ($P < 0.05$)

3.2 Histological Changes:

Figure No (1-3) Cross-section of rat kidney tissue from the negative control group. The typical glomerulus, Bowman's capsule, proximal convoluted tubule, distal tubule, and Bowman's space are observed.

Figure No (3-2) and (3-3) Cross-section of rat kidney tissue from the group administered Thioacetamide via injection at a specified dosage of 200 mg/kg b.w.. Shows glomerular atrophy, widened Bowman's space, destruction of renal tubule walls, and detachment of their epithelial lining and congestion of blood vessels between renal tubules, destruction of renal tubule walls and cellular necrosis.

Figure No (4–3) Cross-section of rat kidney tissue from the group injected with TAA at a dosage of 200 mg/kg body weight and alcoholic extract of Opuntia ficus-indica pulp at 100 mg/kg body weight. Shows the glomerulus, Bowman's capsule, blood congestion, and hemorrhage.

Figure No (5-3) Cross-section of rat kidney tissue from the group received Thioacetamide intraperitoneally at a dose of 200 mg/kg and alcoholic extract of Opuntia ficus-indica peel at 100 mg/kg b.w.. Shows the glomerulus, Bowman's capsule, blood congestion, Bowman's space, and normal structure of renal tubules.

Figure No. (3-6) Cross-section of rat kidney tissue from the group delivered TAA was through injection at a dosage of 200 mg/kg b.w. and nano-extract of Opuntia ficus-indica pulp at 54 mg/kg body weight. Shows normal glomerular structure, Bowman's capsule, and the normal structure of some renal tubules.

Figure No (7-3) Cross-section of rat liver tissue intraperitoneal administration of Thioacetamide (TAA) at a dosage of 200 mg/kg b.w. and nano-extract of Opuntia ficus-indica peel at 50 mg/kg body weight. No apparent damage observed; the glomerulus and tissue appear nearly normal, with the presence of Bowman's capsule, Bowman's space, and normal structure of proximal and distal renal tubules.

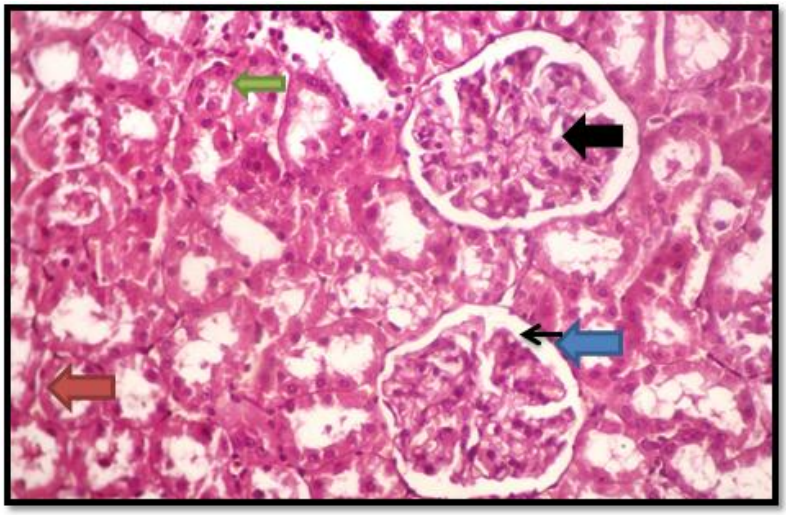

Figure No(3-1) Cross-section of rat kidney tissue from the negative control group. The normal glomerulus ( ), Bowman's capsule ( ), proximal convoluted tubule ( ), distal tubule ( ), and Bowman's space ( ) are observed. (H & E 200X)

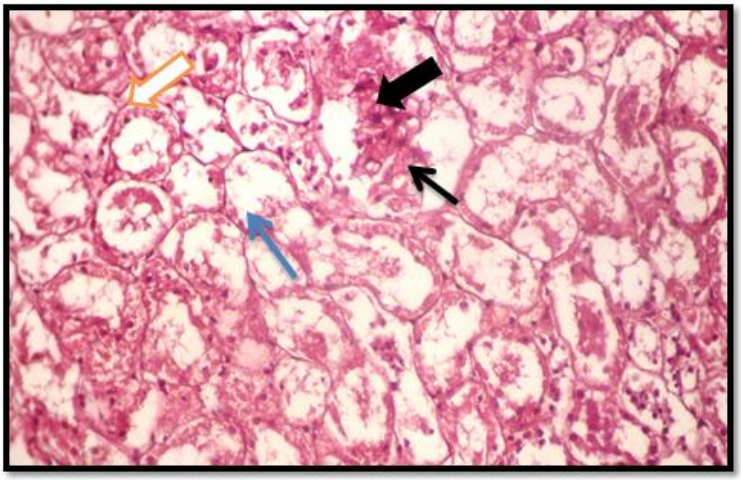

Figure No (3-2) Cross-section of rat kidney tissue from the group Exposed to Thioacetamide at a dose of 200 mg/kg b.w. Shows glomerular atrophy ( ), widened Bowman's space ( ), destruction of renal tubule walls ( ), and detachment of their epithelial lining ( ) (H & E Stain 200X)

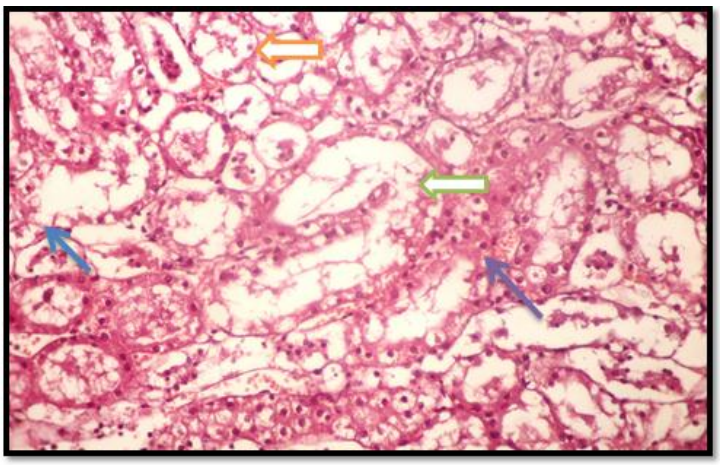

Figure No(3-3) Cross-section of rat kidney tissue from the group injected by Thioacetamide at a dosage of 200 mg/kg body weight. Shows clear degenerative changes in the renal tubules ( ), congestion of blood vessels between renal tubules ( ), destruction of renal tubule walls ( ), detachment of epithelial lining ( ), and cellular necrosis ( ) (H & E Stain 200X)

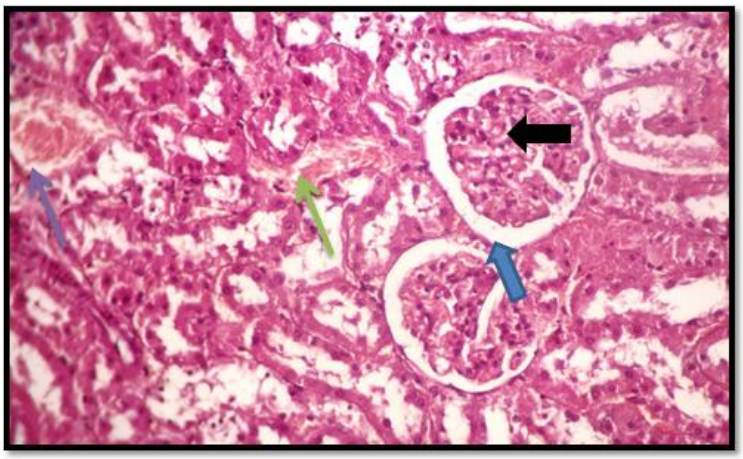

Figure No(3–4) Cross-section of rat kidney tissue from the group Administered Thioacetamide at a concentration of 200 mg per kilogram of body weight and alcoholic extract of Opuntia ficus-indica pulp at 100 mg/kg body weight. Shows the glomerulus ( ), Bowman's capsule ( ), blood congestion ( ), and hemorrhage ( ) (H & E 200X)

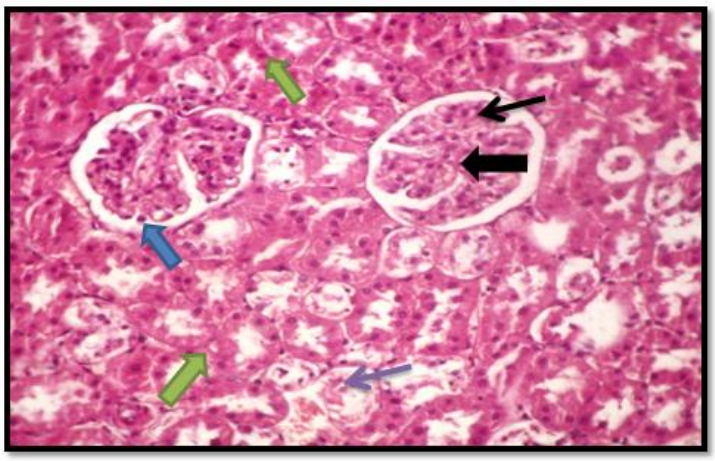

Figure No(3-5) Cross-section of rat kidney tissue from the group Received Thioacetamide treatment at a dosage of 200 mg/kg b.w and alcoholic extract of Opuntia ficus-indica peel at 100 mg/kg body weight. Shows the glomerulus ( ), Bowman's capsule ( ), blood congestion ( ), Bowman's space ( ), and normal structure of renal tubules ( ) (H & E 200X)

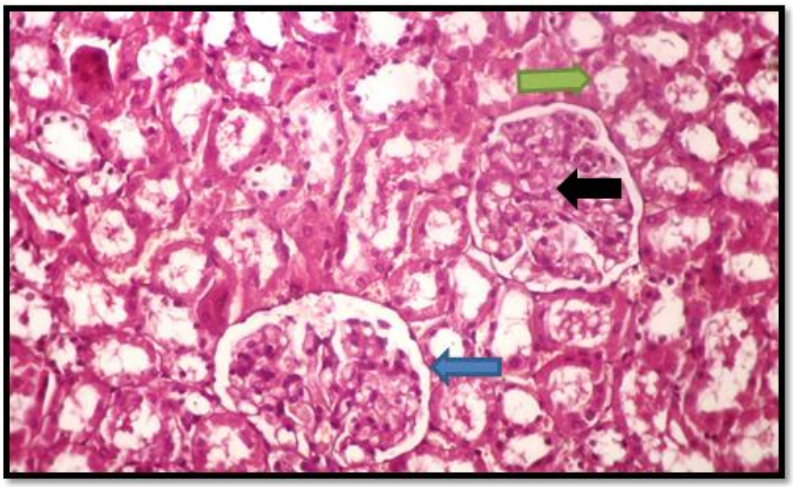

Figure No. (3-6) Cross-section of rat kidney tissue from the group treated with TAA at a dosage of 200 mg/kg b. w. and nano-extract of *Opuntia ficus-indica* pulp at 54 mg/kg body weight. Shows normal glomerular structure ( ), Bowman's capsule ( ), and normal structure of some renal tubules ( ).(H & E 200X)

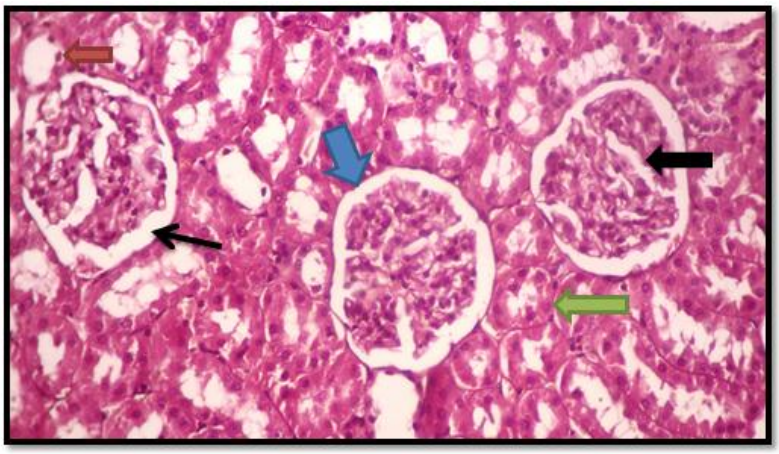

Figure No (3-7) Cross-section of rat liver tissue from the group administered with TAA at a dosage of 200 mg/kg b. w. and nano-extract of Opuntia ficus-indica peel at 50 mg/kg body weight. No apparent damage observed; the glomerulus and tissue appear nearly normal ( ), with presence of Bowman's capsule ( ), Bowman's space ( ), and normal structure of proximal ( ) and distal renal tubules ( ) (H & E Stain 200X)

4. Discussion

The Effect of Thioacetamide, Alcoholic Extract, and Nano-Prickly Pear Fruit Extract on Urea, Creatinine, and Albumin Levels

The results showed that injection with Thioacetamide led to a substantial elevation ($P<0.05$) in urea and creatinine concentrations, while causing a significant decrease ($P<0.05$) in albumin levels. This is consistent with the findings of [17,18]. The kidneys are susceptible to various chemical compounds, causing changes in their function parameters. Impaired renal function is indicated by elevated blood urea and creatinine levels. Oxidative stress, promoting nephron damage through reactive oxygen radicals, significantly contributes to kidney disease development [19]. Elevated urea and creatinine levels may be due to changes in filtration rate, GFR, tubular reabsorption, and renal blood flow [20]. Thioacetamide, a hepatotoxic substance, causes severe liver damage, necrosis, fibrosis, and cirrhosis, directly impacting kidney function through hepatorenal syndrome (HRS) [21]. Thioacetamide (TAA) exposure causes severe nephrotoxicity, causing oxidative stress and inflammation, leading to kidney function deterioration [22]. TAA metabolism produces reactive oxygen species (ROS) and secondary metabolites, damaging renal tubular cell components like lipids, proteins, and DNA. This deterioration is exacerbated by TAA's metabolic processes [23]. Exposure to thioacetamide (TAA) leads to severe nephrotoxicity by inducing oxidative stress and an inflammatory response, which are major factors contributing to the deterioration of kidney function. Elevated inflammatory cytokines increase renal capillary permeability, impeding filtration and accumulating waste products. This damage also damages tubular cells, affecting their ability to reabsorb essential substances and increasing blood concentrations of urea and creatinine. Both factors contribute to the worsening of renal failure [24]. Low albumin levels can indicate various conditions, including chronic liver diseases, kidney disease, and cancer. Inflammatory conditions often lead to albumin deficiency, as factors like thioacetamide, which damages hepatocytes and inhibits protein synthesis, can reduce albumin production [25]. Thioacetamide also stimulates the production of reactive oxygen species, leading to oxidative stress that damages mitochondria and hepatocytes. It also activates hepatic stellate cells, leading to collagen accumulation and liver fibrosis. As fibrosis progresses, the liver's ability to synthesise albumin declines, resulting in nonfunctional fibrous tissue replacing healthy hepatocytes [26]. Chronic kidney injury can also lead to kidney fibrosis, as collagen and other proteins that contribute to fibrous tissue formation are increased. These effects may exacerbate the decline in albumin levels [26.23].

The findings of the present investigation indicated that treatment with alcoholic and nano-

extracts of prickly pear pulp and peel resulted in a reduction in urea and creatinine concentrations, consistent with the results of studies [27,28,29]. The reduction in creatinine and urea concentrations in albino rats administered with alcoholic and nano-extracts of prickly pear, which were induced by thioacetamide (TAA) nephrotoxicity, is attributed to the role of active compounds such as phenolic compounds, flavonoids, and vitamin C, which are powerful antioxidants. These antioxidants help reduce oxidative stress, which can damage kidney cells and impair their function [30]. Prickly pear extract has antioxidant and anti-inflammatory properties, which help reduce kidney tissue damage and improve kidney function. It contains flavonoids like quercetin, isorhamnetin, kaempferol, and luteolin, which reduce oxidative stress in kidney cells and limit damage from toxins or infections. Quercetin inhibits enzymes like 15-lipoxygenase-1 and cyclooxygenase, which are key to kidney damage. Vitamin C (ascorbic acid) and tocopherols also play a role in renal protection, acting as inhibitors of N-Acetyl-β-glucosaminidase (NAG) and reducing free radical production, thus preventing kidney tissue damage and improving kidney function [29]. Prickly pear contains active compounds that can decrease protein breakdown, reducing urea production. as one of the causes of high urea levels is increased protein breakdown in the body [28]. Prickly pear also contains anti-inflammatory properties like betalains, which can improve kidney function by reducing inflammation and maintaining normal levels of urea and creatinine [31.32]. The study found that oral administration of alcoholic and nano-extracts of prickly pear pulp and peel increased albumin levels. This aligns with the findings of a study [33]. which is due to the bioactive compounds in the fruit extract, particularly betalains and phenolic compounds. These compounds have strong antioxidant and cytoprotective properties, helping protect the liver by neutralising harmful free radicals and supporting its natural detoxification processes [34]. Antioxidants like betalains and vitamin C are crucial in liver detoxification and protecting liver cells from damage caused by oxidative stress [35,36].

The Effect of Thioacetamide, Alcoholic Extract, and Nano-Prickly Pear Fruit Extract on Kidney Tissue

The results showed that intraperitoneal injection of thioacetamide led to congestion, inflammation, atrophy, and shrinkage of the glomeruli, indicating a severe inflammatory response. Collapse of the urinary tubules was also observed, with shedding of the cells lining their inner walls, consistent with a study by [37,38]. These effects are attributed to thioacetamide, which causes severe damage to the kidneys [39]. Exposure to thioacetamide manifests a range of structural changes, including renal tubular degeneration, characterized by the death of tubular epithelial cells, as well as damage to the glomeruli, which affects the filtration units in the kidney [21]. It is also characterized by damage to the proximal renal tubules, leading to cell death in the terminal portion of these tubules [40]. Histological examination of kidney tissue showed that treatment with alcoholic and nano-extracts of prickly pear fruit improved kidney tissue, consistent with the study by [31,29]. The renal protective effects of Opuntia ficus-indica fruit extract are largely attributed to its potent antioxidant properties, which arise from its rich content of phenolic compounds, flavonoids, betalains, ascorbic acid, and carotenoids [41]. The presence of specific antioxidant compounds in prickly pear fruit, such as myricetin, quercetin, and luteolin, is a key factor in its ability to protect against toxin-induced kidney damage [31]. Prickly pear has anti-inflammatory properties that can protect the kidneys through several biological mechanisms [42].

Conclusion

Alcoholic and nano-extracts of prickly pear pulp and peel demonstrated clear protective effects against thioacetamide-induced nephrotoxicity by improving renal function (urea, creatinine, and albumin) markers and enhancing kidney tissue improvement. These results support the potential of prickly pear extracts as a natural preventive option, warranting further clinical studies.

References

1. Gu, Y. Y., Liu, X. S., Huang, X. R., Yu, X. Q., & Lan, H. Y. (2020). Diverse role of TGF-β in kidney disease. *Frontiers in cell and developmental biology*, *8*, 123.
2. Korbut, A. I., Romanov, V. V., & Klimontov, V. V. (2023). Urinary markers of tubular injury and renal fibrosis in patients with type 2 diabetes and different phenotypes of chronic kidney disease. *Life*, *13*(2), 343.
3. Begum, Q., Noori, S., & Mahboob, T. (2011). Antioxidant effect of sodium selenite on thioacetamide-induced renal toxicity. *Pakistan Journal of Biochemistry and Molecular Biology*, *44*(1), 21-26.
4. Silva, F. G. (2004). Chemical-induced nephropathy: a review of the renal tubulointerstitial lesions in humans. *Toxicologic pathology*, *32*(2_suppl), 71-84.
5. Al-Kuraishy, H. M., Al-Gareeb, A. L. I. I., & Al-Naimi, M. S. S. (2019). Pomegranate attenuates acute gentamicin-induced nephrotoxicity in Sprague-Dawley rats: The potential antioxidant and anti-inflammatory effects. *Pomegranate*, *12*(3), 484e6.
6. Ghosh S, Sarkar A, Bhattacharyya S, Sil PC (2016) Silymarin protects mouse liver and kidney from thioacetamide induced toxicity by scavenging reactive oxygen species and activating PI3K-Akt pathway. Front Pharmacol 7:481
7. Staňková, P., Kučera, O., Lotková, H., Roušar, T., Endlicher, R., & Červinková, Z. (2010). The toxic effect of thioacetamide on rat liver in vitro. *Toxicology in vitro*, *24*(8), 2097-2103.
8. Zargar, S., Alonazi, M., Rizwana, H., & Wani, T. A. (2019). Resveratrol reverses thioacetamide-induced renal assault with respect to oxidative stress, renal function, DNA damage, and cytokine release in Wistar rats. *Oxidative medicine and cellular longevity*, *2019*(1), 1702959.
9. Kadir, F. A., Kassim, N. M., Abdulla, M. A., & Yehye, W. A. (2013). Effect of oral administration of ethanolic extract of Vitex negundo on thioacetamide-induced nephrotoxicity in rats. *BMC complementary and alternative medicine*, *13*, 1-8.
10. Sairazi, N. S. A. M., Sirajudeen, K. N. S., & Sirajudeen, K. N. S. (2020). Natural Products and Their Bioactive Compounds: Neuroprotective Potentials against Neurodegenerative Diseases. Evidence-based Complementary and Alternative Medicine: eCAM, 2020.
11. Prisa, D. (2021). Opuntia ficus-indica the key plant in climate change: Characteristics, cultivation and uses. *GSC Biol. Pharm. Sci*, *17*(2), 094-105.
12. Sabtain, B., Farooq, R., Shafique, B., Modassar, M., Ranjha, A. N., Mahmood, S., ... & Rubab, Q. (2021). A narrative review on the phytochemistry, nutritional profile and properties of prickly pear fruit. *Open Access J. Biog. Sci. Res*, *7*(7).
13. Sharma, P., & Modi, N. (2023). Qualitative and quantitative phytochemical screening and antioxidant potential of different extracts of Opuntia ficus indica fruits. In *Biological Forum–An International Journal* (Vol. 15, No. 4, pp. 694-701).
14. Bouaouine, O., Bourven, I., Khalil, F., & Baudu, M. (2018). Identification of functional groups of Opuntia ficus-indica involved in coagulation process after its active part extraction. *Environmental Science and Pollution Research*, *25*, 11111-11119.
15. Kulkarni, S. J., Maske, K. N., Budre, M. P., & Mahajan, R. P. (2012). Extraction and purification of curcuminoids from Turmeric (Curcuma longa L.). International Journal of Pharmacology and Pharmaceutical Technology, 1(2), 81–84.
16. Bashi, A. M., Hussein, M. Z., Zainal, Z., & Tichit, D. (2013). Synthesis and controlled release properties of 2, 4-dichlorophenoxy acetate–zinc layered hydroxide nanohybrid. Journal of Solid State Chemistry, 203, 19–24.

17. Abdelhameed, M., Bashandy, S., Ibrahim, F., Morsy, F., Farid, O., & Elbaset, M. (2022). The Pivotal role of Cerium oxide nanoparticles in thioacetamide-induced hepatorenal injury in rat. *Egyptian Journal of Chemistry*, *0*(0), 0. https://doi.org/10.21608/ejchem.2022.115482.5242

18. Ebhohon, S. O., Asoya, E. V., Kalu, M., Ugochukwu, O. L., & Inyama, A. J. (2024). Protective Effects of Aqueous-Ethanol Leaf Extract of Justicia Carnea Lindl. and Silymarin on Thioacetamide-Induced Hepatorenal Injury in Rats. *Pharmacology and Toxicology of Natural Medicines (ISSN 2756-6838)*, *4*(1–2), 1–9. https://doi.org/10.52406/ptnm.v4i1-2.87

19. Zeghib, K., & Boutlelis, D. A. (2021). Food Additive (Sodium benzoate)- induced Damage on Renal Function and Glomerular Cells in Rats; Modulating Effect of Aqueous Extract of Atriplex halimus L. Iranian Journal of Pharmaceutical Research: IJPR, 20(1), 296.

20. Gounden, V., Bhatt, H., & Jialal, I. (2024). Renal function tests. In *StatPearls [Internet]*. StatPearls Publishing.

21. El-Hameed, S. A., Ibrahim, I., Awadin, W., & El-Shaieb, A. (2024). Assessment of single and combined administration of ubiquinone and lactoferrin on histopathology, ultrastructure, oxidative stress, and WNT4 expression gene induced by thioacetamide on hepatorenal system of adult male rats. *Beni-Suef University Journal of Basic and Applied Sciences*, *13*(1), 41. https://doi.org/10.1186/s43088-024-00494-w

22. Zargar, S., Alonazi, M., Rizwana, H., & Wani, T. A. (2019). Resveratrol Reverses Thioacetamide-Induced Renal Assault with respect to Oxidative Stress, Renal Function, DNA Damage, and Cytokine Release in Wistar Rats. *Oxidative Medicine and Cellular Longevity*, *2019*, 1–8. https://doi.org/10.1155/2019/1702959

23. Bashandy, S. a. E., Awdan, S. a. E., Mohamed, S. M., & Omara, E. a. A. (2020). Allium porrum and Bauhinia Variegata Mitigate Acute Liver Failure and Nephrotoxicity Induced by Thioacetamide in Male Rats. *Indian Journal of Clinical Biochemistry*, *35*(2), 147–157. https://doi.org/10.1007/s12291-018-0803-5

24. Jorgačević, B., Stanković, S., Filipović, J., Samardžić, J., Vučević, D., & Radosavljević, T. (2022). Betaine modulating MIF-mediated oxidative stress, inflammation and fibrogenesis in thioacetamide-induced nephrotoxicity. Current Medicinal Chemistry, 29(31), 5254-5267.

25. Sheinenzon, A., Shehadeh, M., Michelis, R., Shaoul, E., & Ronen, O. (2021). Serum albumin levels and inflammation. *International journal of biological macromolecules*, *184*, 857-862.

26. Zhang, H., & Xu, J. (2024). Unveiling thioacetamide-induced toxicity: Multi-organ damage and omitted bone toxicity. *Human & Experimental Toxicology*, *43*. https://doi.org/10.1177/09603271241241807

27. McKay, K. A. J. (2025). Antidiabetic properties of Prickly Pear (Opuntia Ficus-Indica) fruit extract. *The Undergraduate Research Journal*, *10*(1), 11.

28. Taher, N. H. M. (2023). The effect of aqueous and alcoholic extract of Opuntia ficus indica on biochemical parameters and kidney function in rats infected with echinococcosis. *GSC Biological and Pharmaceutical Sciences*, *25*(2), 244–248. https://doi.org/10.30574/gscbps.2023.25.2.0488

29. Villanueva-Huallpa, J. A., Ruelas, M. G., & Huamán-Gutierrez, O. G. (2025). Efecto nefroprotector del jugo de Opuntia ficus indica variedad morada en ratas inducidas a daño renal por gentamicina. *Nutrición Clínica Y Dietética Hospitalaria/Nutrición Clínica, Dietética Hospitalaria*, *45*(1). https://doi.org/10.12873/451villanueva

30. Madrigal-Santillán, E., Portillo-Reyes, J., Madrigal-Bujaidar, E., Sánchez-Gutiérrez, M., Mercado-Gonzalez, P., Izquierdo-Vega, J., Vargas-Mendoza, N., Álvarez-González, I., Fregoso-Aguilar, T., Delgado-Olivares, L., Morales-González, Á., Anguiano-Robledo, L., &

Morales-González, J. (2022). Opuntia genus in Human Health: A Comprehensive Summary on Its Pharmacological, Therapeutic and Preventive Properties. Part 1. *Horticulturae*, *8*(2), 88. https://doi.org/10.3390/horticulturae8020088

31. Okur, M. E., Ayla, Ş., Karadağ, A. E., Polat, D. Ç., Demirci, S., & Seçkin, İ. (2020). Opuntia ficus indica fruits ameliorate cisplatin-induced nephrotoxicity in mice. *Biological and Pharmaceutical Bulletin*, *43*(5), 831-838. https://doi.org/10.1248/bpb.b19-01044
32. El-Said, N. M., Nagib, A. I., Rahman, Z. A., & Deraz, S. F. (2011). Prickly pear [Opuntia ficus-indica (L.) Mill] peels: chemical composition, nutritional value, and protective effects on liver and kidney functions and cholesterol in rats. *Funct. Plant Sci. Biotechnol*, *5*(1), 30-35.
33. Kim, K. T., Leem, K. H., & Jung, J. H. (2024). Double-blind Randomized placebo-controlled Trials on controlling blood glucose level using the extract from Opuntia ficus-indica var. saboten. *The Journal of Korean Medicine*, *45*(4), 84-98.
34. Vieira, A. C. A., Ferreira, F. D. S., Araújo, J. M. D. D., Dutra, L. M. G., Batista, K. S., Cordeiro, A. M. T. D. M., & Aquino, J. D. S. (2024). Exploring the Potential Hepatoprotective Properties of Cactus (Cactaceae) in Liver Health and Disease Management: A Brief Review. Livers, 4(2), 287-313.
35. Wang, J., Rani, N., Jakhar, S., Redhu, R., Kumar, S., Kumar, S., Kumar, S., Devi, B., Simal-Gandara, J., Shen, B., & Singla, R. K. (2023). Opuntia ficus-indica (L.) Mill. - anticancer properties and phytochemicals: current trends and future perspectives. *Frontiers in Plant Science*, *14*. https://doi.org/10.3389/fpls.2023.1236123
36. Hafeez, H., Israr, B., Butt, M. S., & Faisal, M. N. (2024). Therapeutic Intervention of Opuntia Ficus Indica (L.) Fruit and Seed Powder against CCl 4-Induced Acute Liver Injury in Wistar Rats. Pakistan Veterinary Journal, 44(2).
37. Lim, J., Jung, W., Kim, W., Moon, K., & Sul, D. (2022). Nephrotoxicity evaluation and proteomic analysis in kidneys of rats exposed to thioacetamide. *Scientific Reports*, *12*(1). https://doi.org/10.1038/s41598-022-11011-3
38. Elbaset, M. A., Mohamed, B. M. S. A., Gad, S. A., Afifi, S. M., Esatbeyoglu, T., Abdelrahman, S. S., & Fayed, H. M. (2023). Erythropoietin mitigated thioacetamide-induced renal injury via JAK2/STAT5 and AMPK pathway. *Scientific Reports*, *13*(1). https://doi.org/10.1038/s41598-023-42210-1
39. Radwan, A. M., Karhib, M., Fatoh, S. A., & Tousson, E. (2023). Curcumin alleviates Thioacetamide-Induced kidney toxicity in rats: enhancing antioxidant system, and attenuating oxidative stress, DNA damage, and inflammation. *Biomedical & Pharmacology Journal*, *16*(1), 441–450. https://doi.org/10.13005/bpj/2625
40. El-Hameed, S. A., Ibrahim, I., Awadin, W., & El-Shaieb, A. (2023). Thioacetamide: definition, exposure, hepatic and renal toxicity. *Mansoura Veterinary Medical Journal*, *24*(4). https://doi.org/10.35943/2682-2512.1217
41. Giraldo-Silva, L., Ferreira, B., Rosa, E., & Dias, A. C. P. (2023). Opuntia ficus-indica Fruit: A Systematic Review of Its Phytochemicals and Pharmacological Activities. *Plants*, *12*(3), 543. https://doi.org/10.3390/plants12030543
42. Habtemariam, S. (2019). The chemical and pharmacological basis of prickly pear cactus (Opuntia species) as potential therapy for type 2 diabetes and obesity. In *Elsevier eBooks* (pp. 435–472). https://doi.org/10.1016/b978-0-08-102922-0.00013-4