

# Nephroprotective Role of Aqueous Extract of *Citrullus Lanatus* Seed in Alcohol-Induced Renal Dysfunction in Wistar Rats

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DOI: <https://doi.org/10.51244/IJRSI.2025.12120036>

Received: 18 December 2025; Accepted: 25 December 2025; Published: 03 January 2026

## ABSTRACT

Chronic alcohol consumption induces renal oxidative stress, tubular degeneration, and glomerular dysfunction. Plant-based antioxidants such as *Citrullus lanatus* (watermelon) seeds possess bioactive compounds that may protect against nephrotoxicity (Ifudu and Adewale, 2014; Varga et al., 2017). This study evaluated the nephroprotective effect of aqueous extract of *Citrullus lanatus* seed (AECL) on alcohol-induced renal dysfunction in Wistar rats. Thirty male Wistar rats (130–150 g) were divided into five groups (n = 6): Group I (normal control) received feed and water only; Group II (alcohol control) received ethanol (1 mL/day) for 2 weeks; Group III received AECL (500 mg/kg) only; Group IV received ethanol + AECL (500 mg/kg); and Group V received ethanol + AECL (1000 mg/kg). All treatments were administered orally for 6 weeks. Serum levels of urea, creatinine, uric acid, and electrolytes (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>) were determined using standard colorimetric methods. Data were analyzed using one-way ANOVA and LSD post-hoc test, with  $p \leq 0.05$  considered significant. Alcohol significantly increased serum urea, creatinine, and uric acid ( $p < 0.05$ ) compared to control. Treatment with AECL reduced these parameters dose-dependently. The 1000 mg/kg extract produced values closest to normal. Electrolyte levels were also stabilized in treated groups. Aqueous extract of *Citrullus lanatus* seed confers nephroprotection against alcohol-induced renal toxicity, likely through antioxidant and membrane-stabilizing actions.

**Keywords:** *Citrullus lanatus*, nephrotoxicity, ethanol, renal biomarkers, oxidative stress, Wistar rat

## INTRODUCTION

The kidney plays a crucial role in homeostasis, excretion, and detoxification. Chronic alcohol intake has been shown to induce renal dysfunction by increasing oxidative stress, generating free radicals, and promoting tubular degeneration (Ifudu and Adewale, 2014; Varga et al., 2017). These reactive oxygen species (ROS) cause lipid peroxidation and damage to glomerular and tubular cells, leading to elevated urea and creatinine levels. Alcohol-related nephrotoxicity also disrupts electrolyte balance, reduces glomerular filtration rate, and alters the renal antioxidant defense system (Cheungpasitporn et al., 2015; Kawamoto et al., 2021). Plant-based antioxidants have gained attention as potential therapeutic agents against renal oxidative stress. *Citrullus lanatus* (watermelon) seeds are rich in flavonoids, phenolics, tannins, and saponins—compounds known to possess antioxidant, anti-inflammatory, and detoxifying effects (Deshmukh, Jain and Tambe, 2015; Ullah et al., 2020). Although previous studies have demonstrated the hepatoprotective role of *C. lanatus*, its nephroprotective efficacy against alcohol-induced renal injury remains less explored. This study therefore investigated the protective effects of aqueous *C. lanatus* seed extract on alcohol-induced renal dysfunction in Wistar rats.

## MATERIALS AND METHODS

### Location of Study

The study was conducted in the Animal House, Department of Human Physiology, Faculty of Basic Medical Sciences, Chukwuemeka Odumegwu Ojukwu University, Uli Campus, Anambra State, Nigeria.

### Materials

The materials used include *Citrullus lanatus* seeds, thirty (30) male Wistar rats, Randox reagent kits (England), Pyrex beakers (Techmel, USA), measuring cylinders (MINGHE), 2 mL hypodermic syringes, an electronic weighing balance (Mettler M311L, China), oral cannula, microscope slides, Olympus XSZ-107BN microscope, and Whatman qualitative filter paper No. 1 (Sigma Aldrich WHA1001042). Additional items included distilled water, standard plastic cages, cotton wool (KENS LINT, Benin City, Nigeria), latex hand gloves (Supermax Gloves, Selangor, Malaysia), chloroform (Guangdong Guandgua Chemical Factory Co. Ltd., Shatou, China), Vital Grower feed (Jos, Nigeria), dissecting kits, automatic water distiller (SZ-1 Search Tech Instrument), Nexus refrigerator, rotary evaporator (TT-52; Techmel & Techmel, USA), UV-VIS 752N spectrophotometer (Shanghai Yoke Instrument Co., Ltd., China), and thermostat oven (DHG-9023A, PEC MEDICAL, USA).

### Extraction procedure

Fresh *Citrullus lanatus* (watermelon) seeds were obtained, washed thoroughly with clean water, and air-dried at room temperature to remove moisture. The dried seeds were ground into coarse powder using a local grinder. Exactly 250 g of the powdered seed was soaked in 1500 ml of lukewarm distilled water and macerated for 24 hours with intermittent shaking to enhance extraction. The mixture was first sieved using a clean muslin cloth and then filtered through Whatman No. 1 filter paper into a clean glass container. The filtrate obtained was concentrated using a rotary evaporator and further dried in a thermostat oven at 45°C to yield a gel-like extract. The final extract was stored in an airtight container and preserved in a refrigerator until required for experimental use.

### Experimental design

The animals were randomly divided into five (5) groups of six rats each as follows:

Group A (Alcohol control): Received alcohol only.

Group B (Normal control): Received feed and distilled water only.

Group C (Extract control): Received 500 mg/kg of aqueous seed extract of *C. lanatus* (ASCL) only.

Group D (Low-dose treatment): Received alcohol for two weeks followed by 500 mg/kg ASCL for four weeks.

Group E (High-dose treatment): Received alcohol for two weeks followed by 1000 mg/kg ASCL for four weeks.

Alcohol administration was done orally using a cannula to induce renal toxicity. The aqueous seed extract of *Citrullus lanatus* was also administered orally using a cannula for the duration of the treatment. The entire experimental period lasted six (6) weeks.

### Statistical analysis

Data obtained were analyzed using Statistical Package for Social Sciences (SPSS) version 25 (IBM, USA). Results were expressed as mean  $\pm$  standard error of mean (SEM). Statistical differences between groups were determined using one-way analysis of variance (ANOVA) followed by Fisher's Least Significant Difference (LSD) post hoc test. Differences were considered statistically significant at  $p \leq 0.05$ .

## RESULTS

### Relative Kidney Weight

Ethanol administration caused a significant increase ( $p < 0.05$ ) in relative kidney weight, indicating renal stress. AECL treatment at both 500 mg/kg and 1000 mg/kg reduced the increase toward normal.

### Serum Biochemical Parameters

Ethanol significantly elevated urea, creatinine, and uric acid levels, suggesting impaired renal function. AECL administration produced a dose-dependent reduction in these parameters.

**Table 1: Effects of aqueous extract of Citrus lanatus seed on body weight following alcohol induced toxicity**

	Initial body weight (g)	Final body weight (g)	P-value	t-value
	MEAN±SEM	MEAN±SEM		
Group A (1 ml of Alcohol)	175.00±5.40	140.50±5.69	0.008*	6.222
Group B (control)	133.25±2.13	156.00±3.36	0.023*	-4.333
Group C (500 mg/kg of ASCL)	167.40±0.81	177.40±1.96	0.020*	-3.727
Group D (1 ml of Alcohol + 500 mg/kg of ASCL)	167.40±0.81	171.00±2.12	0.202#	-1.527
Group E (1 ml of Alcohol + 1000 mg/kg of ASCL)	147.20±1.24	177.80±1.39	0.000*	-16.948

Data were analyzed using paired t-test. Values were considered significant at  $p \leq 0.05$ . ASCL: aqueous seed extract of Citrus lanatus, \*: significant, #: not significant when compared to group A.

Table 1 result showed a significant decrease in mean body weight in group A when compared to its initial weight ( $p = 0.008$ ). Groups B, C, and E showed a significant increase in body weight ( $p = 0.023$ ,  $p = 0.020$ ,  $p = 0.000$ ), while group D showed no significant difference ( $p = 0.202$ ) but indicated an increasing trend when compared to group A.

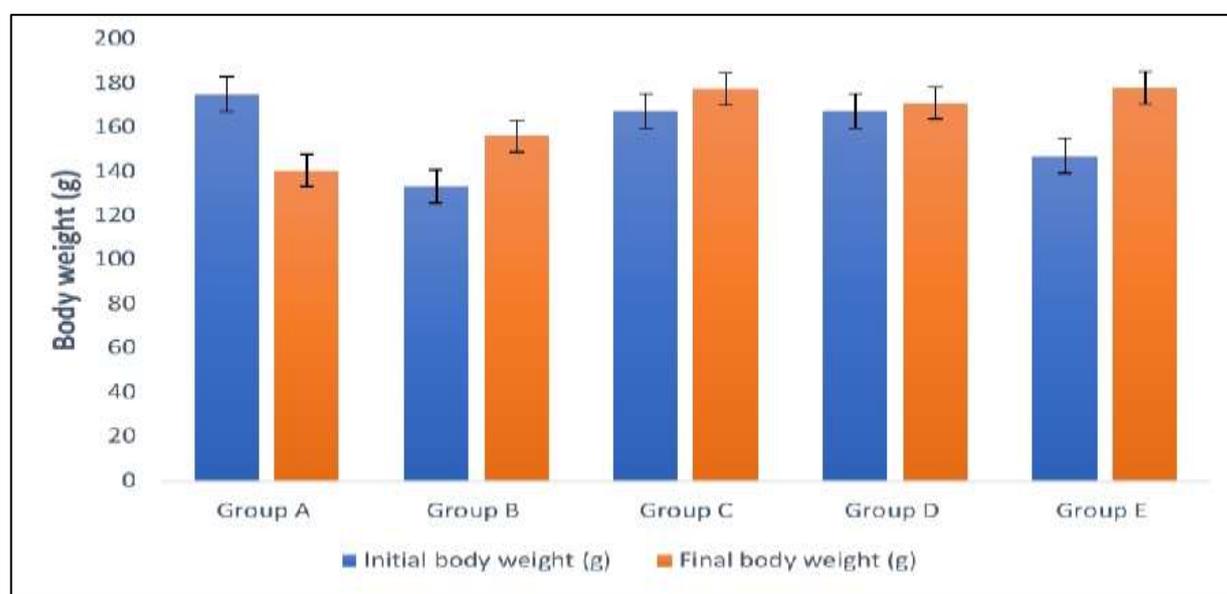


Fig 1: Effects of aqueous extract of Citrus lanatus seed on body weight following alcohol induced toxicity

**Table 2: Effects of aqueous extract of Citrus lanatus seed on relative kidney weight following alcohol-induced toxicity**

	Relative kidney weight (g)
	MEAN±SEM
Group A (1 ml of Alcohol)	0.56±0.01
Group B (control)	0.39±0.02*
Group C (500 mg/kg of ASCL)	0.35±0.03*
Group D (1 ml of Alcohol + 500 mg/kg of ASCL)	0.38±0.02*
Group E (1 ml of Alcohol + 1000 mg/kg of ASCL)	0.36±0.00*
<b>P-value</b>	0.001
<b>F-value</b>	13.403

Data were analyzed using ANOVA followed by post hoc LSD multiple comparison. Values were considered significant at  $p \leq 0.05$ . ASCL: aqueous seed extract of Citrullus lanatus, : significant, #: not significant when compared to group A.

Table 2 result showed a significant increase in relative kidney weight in group A compared to group B ( $p = 0.003$ ), while groups C, D, and E ( $p = 0.001$ ,  $p = 0.002$ ,  $p = 0.001$ ) showed a significant decrease relative to group A.

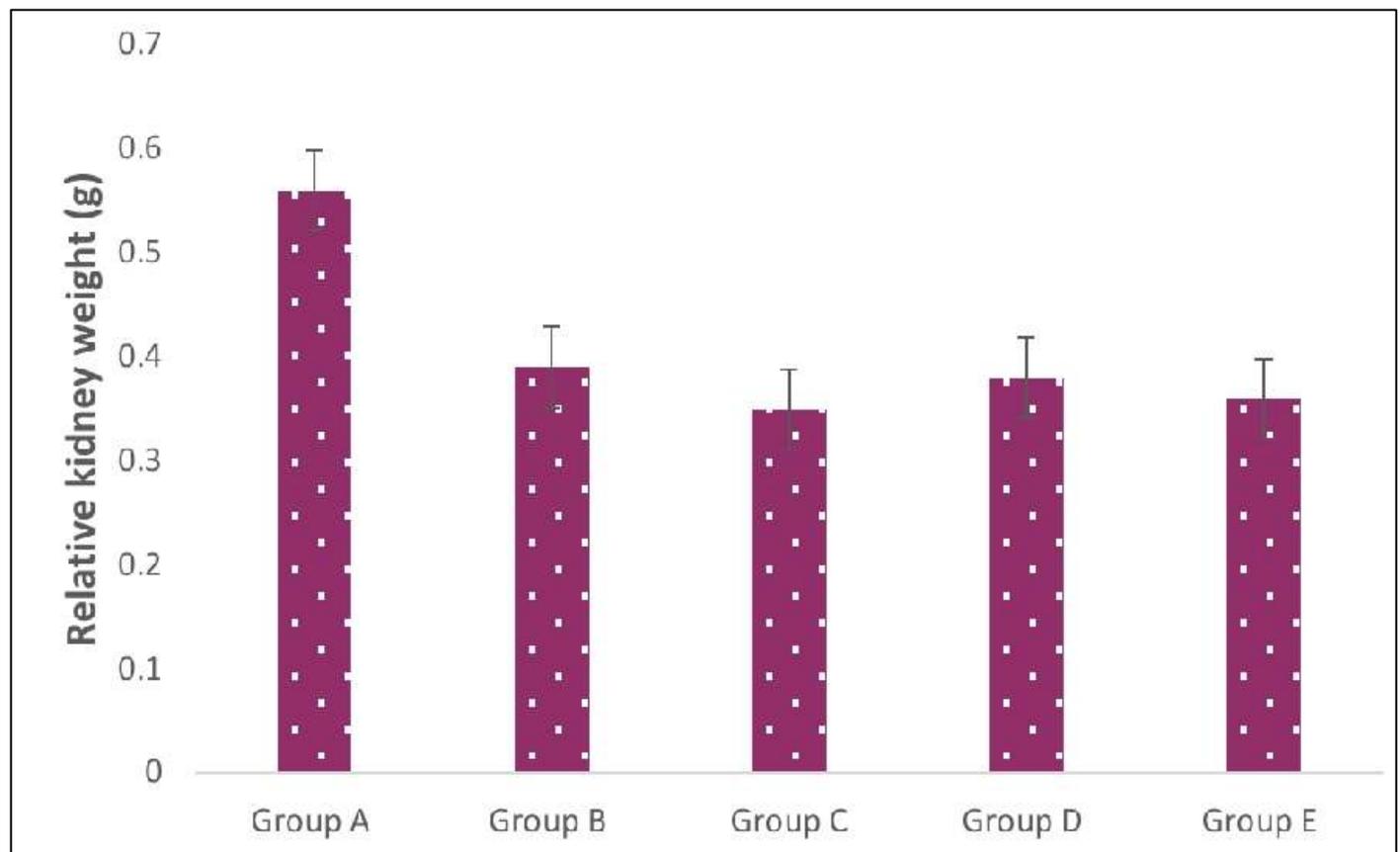


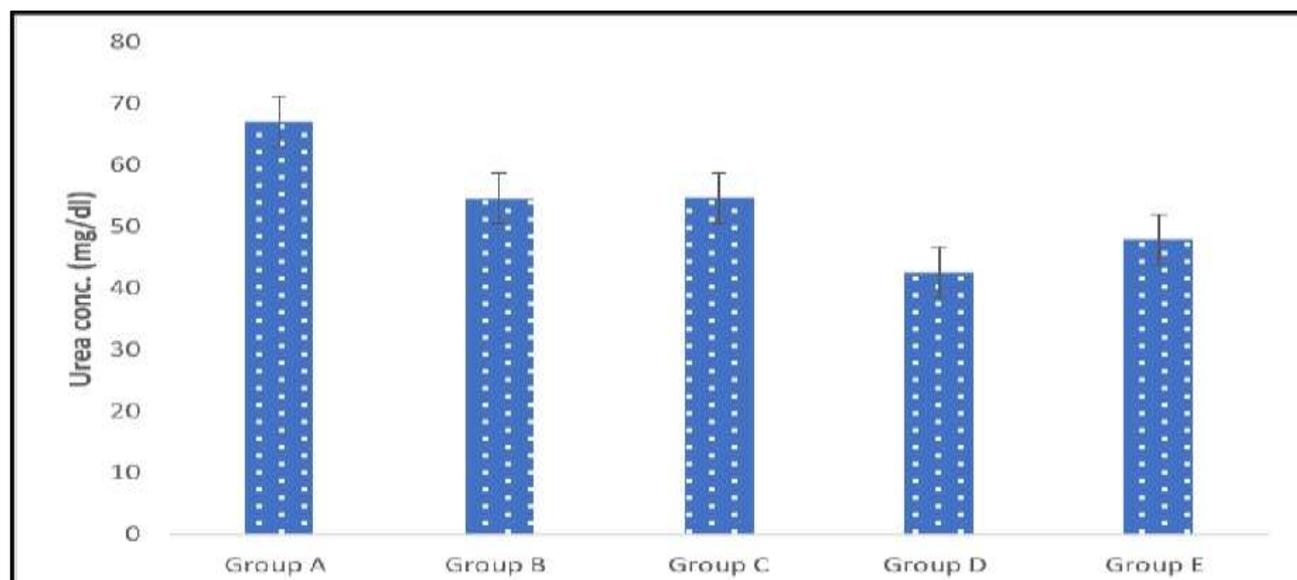
Fig 2 effect of aqueous extract of Citrus lanatus seed on relative kidney weight following alcohol-induced toxicity.

**Table 3: Effects of aqueous extract of Citrulus lanatus seed on urea, uric, and creatinine levels following alcohol-induced toxicity**

	Urea conc. (mg/dl)	Uric acid conc. (mg/dl)	Creatinine conc. (mg/dl)
	MEAN±SEM	MEAN±SEM	MEAN±SEM
Group A (1 ml of Alcohol)	67.18±0.68	6.13±0.24	0.22±0.06
Group B (control)	54.65±0.25*	3.26±0.18*	0.10±0.00*
Group C (500 mg/kg of ASCL)	54.70±0.80*	3.00±0.55*	0.11±0.01*
Group D (1 ml of Alcohol + 500 mg/kg of ASCL)	42.69±1.41*	2.81±0.72*	0.11±0.02*
Group E (1 ml of Alcohol + 1000 mg/kg of ASCL)	48.01±1.34*	2.83±0.63*	0.09±0.01*
P-value	0.000	0.004	0.054
F-value	8.443	7.662	3.159

Data were analyzed using ANOVA followed by post hoc LSD multiple comparison. Values were considered significant at  $p \leq 0.05$ . ASCL: aqueous seed extract of Citrullus lanatus, #: significant, #: not significant when compared to group A.

Table 3 result showed a significant increase in urea level in group A compared to B ( $p = 0.000$ ). Groups C, D, and E ( $p = 0.001$ ,  $p = 0.000$ ,  $p = 0.001$ ) showed significant decreases relative to group A. Uric acid concentration also increased significantly in group A compared to B ( $p = 0.018$ ), while groups C, D, and E ( $p = 0.010$ ,  $p = 0.007$ ,  $p = 0.007$ ) showed significant reductions compared to group A. Creatinine levels increased significantly in group A compared to B ( $p = 0.020$ ), while groups C, D, and E ( $p = 0.020$ ,  $p = 0.026$ ,  $p = 0.013$ ) demonstrated significant decreases relative to group A.



**Fig 3: Effects of aqueous extract of Citrulus lanatus seed on urea levels following alcohol-induced toxicity.**

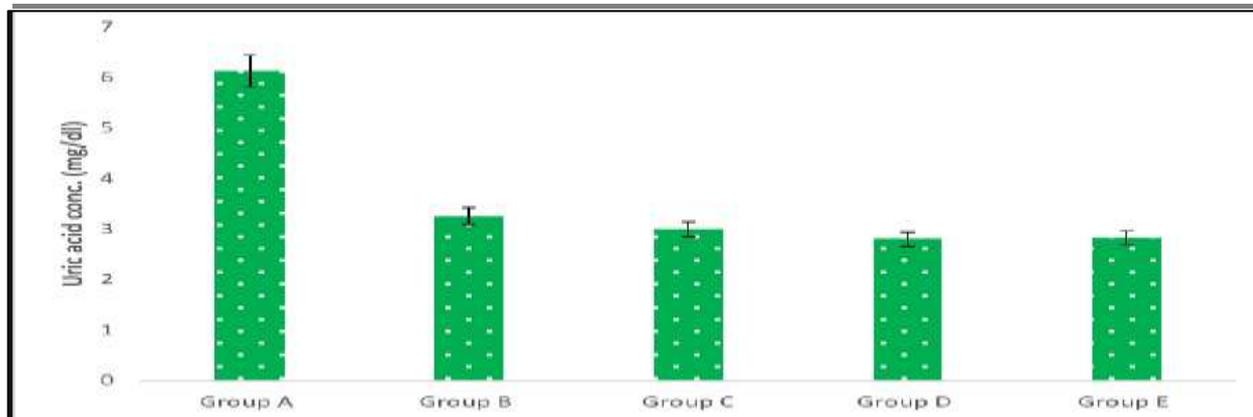


Fig 4: Effects of aqueous extract of Citrus lanatus seed on uric acid concentration following alcohol-induced toxicity.

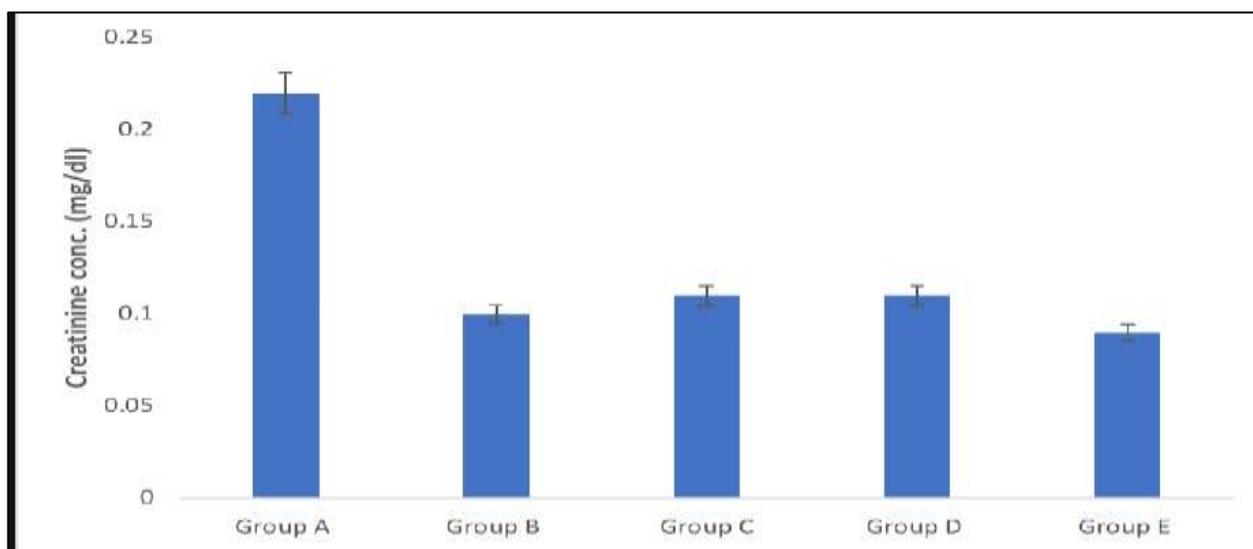


Fig 5: Effects of aqueous extract of Citrus lanatus seed creatinine levels following alcohol-induced toxicity.

**Table 4: Phytochemical Analysis of C. lanatus seed**

Phytochemicals	Reference
Phenols	++
Tannins	++
Flavonoids	+++
Glycosides	+
Saponins	+
Steroids	+

## DISCUSSION

The present study evaluated the nephroprotective role of aqueous extract of Citrullus lanatus seed against alcohol-induced renal dysfunction in Wistar rats. Chronic alcohol administration resulted in marked renal impairment, as demonstrated by significant increases in relative kidney weight and elevated serum urea, creatinine, and uric acid levels. These findings indicate compromised renal structural and functional integrity

and are consistent with earlier reports that prolonged alcohol exposure induces oxidative stress-mediated glomerular and tubular damage (Ifudu and Adewale, 2014; Cheungpasitporn et al., 2015). The significant increase in relative kidney weight observed in the alcohol control group suggests renal inflammation, cellular swelling, and possible congestion arising from toxic injury. Such changes have been attributed to oxidative damage and inflammatory responses within renal tissues following ethanol metabolism. Treatment with aqueous *Citrullus lanatus* seed extract significantly reduced relative kidney weight toward normal values, indicating attenuation of alcohol-induced renal stress and preservation of renal morphology. Elevated serum urea and creatinine levels are classical indicators of impaired glomerular filtration and reduced renal excretory capacity. In the present study, alcohol administration significantly increased these biomarkers, reflecting renal dysfunction. The dose-dependent reduction of urea and creatinine following extract treatment suggests improvement in glomerular filtration and tubular handling of nitrogenous waste products. Similarly, the reduction in uric acid levels indicates enhanced renal clearance and restoration of renal metabolic balance. These observations agree with previous studies that reported nephroprotective effects of *Citrullus lanatus* seed extract in chemically induced renal injury models (Omotoso and Osadiaye, 2018; Daniel et al., 2021). The nephroprotective effects observed may be attributed to the phytochemical constituents identified in the extract, particularly flavonoids, phenolic compounds, and tannins. These compounds possess strong antioxidant properties and are known to scavenge reactive oxygen species generated during alcohol metabolism. By reducing oxidative stress and lipid peroxidation, the extract likely stabilizes renal cell membranes and prevents further cellular damage (Deshmukh et al., 2015; Ullah et al., 2020). The improvement in body weight observed in extract-treated groups further supports the protective role of *Citrullus lanatus* seed extract. Alcohol-induced weight loss is often associated with metabolic imbalance and reduced nutrient utilization. The reversal of this effect suggests that the extract may mitigate systemic toxicity and improve overall metabolic status. Overall, the findings of this study demonstrate that aqueous *Citrullus lanatus* seed extract effectively ameliorates alcohol-induced renal dysfunction by restoring renal biomarkers and reducing renal hypertrophy. This supports the hypothesis that the extract confers nephroprotection primarily through antioxidant and protective biochemical mechanisms

## CONCLUSION

This study demonstrates that chronic alcohol administration induces significant renal dysfunction, evidenced by increased relative kidney weight and elevated serum urea, creatinine, and uric acid levels in Wistar rats. Treatment with aqueous extract of *Citrullus lanatus* seed effectively attenuated these alcohol-induced alterations in a dose-dependent manner, with the higher dose showing greater renoprotective efficacy. The normalization of renal biomarkers and improvement in body and kidney weight indices indicate preservation of renal structural and functional integrity. These protective effects are likely mediated through the antioxidant and membrane-stabilizing actions of the extract's bioactive phytochemicals, particularly flavonoids and phenolic compounds. Overall, the findings support the potential of aqueous *Citrullus lanatus* seed extract as a natural nephroprotective agent against alcohol-induced renal injury and provide a scientific basis for its possible therapeutic application in managing oxidative stress-related kidney dysfunction.

## RECOMMENDATIONS

Further studies should be carried out to identify the active compounds in *Citrullus lanatus* seeds responsible for the observed nephroprotective effects. Histological examination of kidney tissues is recommended to support the biochemical findings. Future research should also investigate different doses and longer treatment durations to better understand the safety and effectiveness of the extract. In addition, studies involving other models of kidney injury and eventual clinical studies in humans are recommended to validate the potential use of *Citrullus lanatus* seed extract in the prevention and management of alcohol-induced renal damage.

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