Research Article

Therapeutic administration of *Convolvulus oxyphyllus* Extract Mitigates Ehrlich Ascites Carcinoma–Associated Renal Dysfunction Through Redox Homeostasis Restoration in Female Mice

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Abstract | The Ehrlich ascitic carcinoma (EAC) model consistently induces oxidative damage to the kidneys. Tumour-related kidney damage may be mitigated by *Convolvulus oxyphyllus* extract (COE), which contains antioxidant bioactive compounds. To examine the nephroprotective and antioxidant effects of COE against EAC in female mice, forty female Swiss albino mice were divided into four groups (n= 10 each): control, COE-only (25 mg/kg/day), EAC-bearing, and EAC + COE-treated. EAC was induced via intraperitoneal injection. The first COE treatment (25 mg/kg/day, oral gavage) began 24 hours after tumour inoculation and continued for fourteen (14) consecutive days. Serum urea, creatinine, and electrolyte levels were measured. Histopathological analysis was performed with haematoxylin and eosin staining. Elevated serum urea and creatinine levels, electrolyte disturbances, and renal dysfunction were more pronounced in EAC-bearing mice compared to controls ($p < 0.05$). Histopathology revealed significant degeneration of glomeruli and tubules. COE treatment improved electrolyte levels and significantly reduced serum urea, and creatinine compared to untreated EAC mice ($p < 0.05$). However, these parameters did not fully normalise relative to controls. The study concluded that COE showed partial nephroprotective effects against EAC-induced renal damage by improving biochemical and histopathological alterations, but without full restoration of normal kidney function.

Keywords | Ehrlich ascites carcinoma, COE, Renal function, Hematoxylin, Eosin

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INTRODUCTION

Renal involvement in the process of cancer is an emerging concern in clinical oncology. This is because cancer is evolving as a systemic metabolic disease that goes beyond the primary tumour and includes other organs, which may include the kidneys. When the tumour grows, systemic metabolic disruptions occur that may damage organs through inflammation, metabolic dysfunction, and oxidative stress (Ozaslan *et al*., 2009). The Ehrlich Ascites Carcinoma (EAC) is one of the common experimental tumour models used to study tumour systemic toxicity. Research using the EAC model has shown that as tumours become more advanced, kidney function progressively

deteriorates, as evidenced by increases in serum urea and creatinine levels, increased oxidative stress, activation of apoptosis, and marked histopathological changes in renal tissues (Rahman *et al*., 2021). This explains the phenomenon of renal tumour toxicity as a result of a tumour, and clinically, it is a significant condition (Chakraborty *et al*., 2015). The persistence of oxidative stress plays a central role in the progression of tumours, as it is the net effect of an overproduction of reactive oxygen species (ROS) that exceeds the body's defence mechanisms against ROS (Alam *et al*., 2016). Ongoing oxidative stress, or redox dysfunction, over many cellular cycles through a series of bioenergetic processes in the mitochondria results in lipid peroxidation, disrupts membranes, and severely reduces both glomerular and tubular kidney function (Medhat *et al*., 2017). In the context of such oxidative stress, there is a documented increase in malondialdehyde (MDA) in renal tissues. MDA is an end product of lipid peroxidation. Other documented changes include reduced superoxide dismutase (SOD) activity and associated renal oxidative injury, both consequences of tumours (Khanam *et al*., 2010). MDA and SOD activity are considered 'signature' biochemical changes that are associated with redox dysregulation and oxidative stress renal injury. Taken together, the documented biochemical changes point to oxidative injury imbalances as the principal cause of the structural and functional renal injuries associated with the tumoral mass. Restoration of damaged tissue integrity and functions disrupted as a consequence of redox imbalances in impacted tissues is vital for the preservation of both form and function of the renal system (Masood *et al*., 2025). Antioxidants are encouraged as possible adjuncts to other treatments. Natural bioactive compounds, such as the phytochemicals from plant sources, are gaining new utility as adjuncts to traditional therapies in the treatment of oxidative cellular damage (Nepomuceno *et al*., 2025). Phytochemicals contain the ability to 'scavenge' free radicals and possess the capacity to enhance both endogenous and exogenous protective mechanisms against free radicals. As well, there is evidence that many phytochemicals can influence key redox-sensitive cellular injury pathways. *Convolvulus oxyphyllus* is a plant used in traditional medicine and is known to contain active ingredients that may have antioxidant and cytoprotective effects (El-Naggar *et al*., 2018). While there is evidence supporting its use as an antioxidant, there is little evidence supporting its use in treating EAC-induced renal dysfunction (Hasan, 2023). Specifically, little is known about its ability to attenuate tumour-related oxidative renal injuries and to normalise functional biomarkers (Al-Whibi *et al*., 2017; Al-Dulimi *et al*., 2025). The goal of this study is to determine the therapeutic effects of *Convolvulus oxyphyllus* extract on EAC-bearing female mice, including its effects on renal oxidative stress, renal function, electrolyte (Urea and Creatinine) levels, and changes in kidney tissues.

MATERIALS AND METHODS

Ehrlich ascites carcinoma (EAC) cell line and inoculation

EAC cells were sourced from the National Cancer Institute (Egypt). Cells were diluted in normal saline sterility and diluted <5% for inoculation by the trypan blue exclusion method. Mice were inoculated with EAC cells intraperitoneally at 2.5 x 10^6 viable EAC cells per 20 g body weight in a volume of 0.2-0.5 mL.

Animals

We received 40 female Swiss albino mice (11-12 weeks; 20-25 g) from National Cancer Institute, Cairo University, Egypt. The animals were housed in polypropylene cages with controlled environmental conditions (25 ± 2 °C, 12-h light/12-h dark cycle) and ad libitum access to food and water.

Experimental design and therapeutic protocol

The mice were randomly divided into four groups (G1–G4; n = 10 per group) using equal allocation (1:1:1:1) by random number assignment. Group 1 served as the control (vehicle). Group 2 received *Convolvulus oxyphyllus* extract (COE) only (25 mg/kg/day). Group 3 consisted of Ehrlich ascites carcinoma (EAC)-bearing mice (tumour control, untreated). Group 4 received EAC + COE (therapeutic group, 25 mg/kg/day). Therapeutic administration of COE was initiated 24 hours after EAC inoculation (Day 1) and continued for 14 consecutive days. The COE dose was selected based on previous studies and acute oral toxicity guidelines (OECD TG 423), with a dosing volume of 10 mL/kg body weight.

Randomisation, blinding, and inclusion/exclusion criteria

Cages were assigned to groups by randomisation. Investigators who performed biochemical assays and scored samples histopathologically were blinded to group assignment using coded sample.

Sample collection

On Day 15 (24 h following the final dosage), the mice were placed under anaesthetic using sodium pentobarbital (≥ 100 mg/kg, i.p.) and euthanised using the exsanguination method. Blood samples were taken from the inferior vena cava and placed into heparinised tubes. These tubes were subsequently centrifuged at 3,000 g for 20 minutes, and the resulting plasma/serum samples were stored at −20 °C. The kidneys were removed, rinsed in ice-cold saline, blotted dry, and weighed. One kidney was preserved in 10% neutral buffered formalin and sent for histological examination, while the other was snap-frozen at −80 °C for analysis of oxidative stress.

Table 1: Changes in kidney functions and Electrolytes level in different groups.

Parameters	Control	CoE	EAC	EAC+CoE
Creatinine (mg/dl)	1.70 ± 1.22$^{\#}$	1.75 ± 1.33$^{\#}$	3.08 ± 1.22*	2.66 ± 3.33$^{\#*}$
Urea (mg/dl)	41.7 ± 2.11$^{\#}$	39.7 ± 5.11$^{\#}$	55.9 ± 6.11*	48.7 ± 7.11$^{\#}$
Na^{+} (mmol/l)	141.6 ± 4.11$^{\#}$	147.4 ± 8.4$^{\#}$	119.3 ± 8.1*	124.1 ± 8.1$^{\#}$
K^{+} (mmol/l)	6.41 ± 1.12$^{\#}$	5.12 ± 2.32$^{\#}$	7.66 ± 1.33*	6.11 ± 2.22$^{\#*}$
Ca^{++} (mmol/l)	3.11 ± 2.01$^{\#}$	3.33 ± 1.11$^{\#}$	2.33 ± 2.26*	2.21 ± 1.37$^{\#*}$
Cl^{-} (mmol/l)	113.2 ± 5.1$^{\#}$	109.2 ± 8.1$^{\#}$	129.3 ± 9.2*	121.2 ± 12.9$^{\#*}$

Data are expressed as mean ± S.E of 10 observations. (*) and (#) indicate significant differences at $p < 0.05$ compared to the control and EAC groups, respectively.

Renal function biomarkers and electrolytes

Serum urea and creatinine were measured with commercial diagnostic kits according to the manufacturer's instructions. Serum electrolytes, including sodium (Na^{+}), potassium (K^{+}), chloride (Cl^{-}), and calcium (Ca^{2+}), were also determined.

Histopathological examination

The kidney tissues fixed in formalin were processed routinely and embedded in paraffin. Then they were subsectioned at 4-5-micron thickness and stained using the hematoxylin and eosin (H & E) method. The sections were blindly examined under a light microscope (model) and the degree of renal injury was estimated using a semi-quantitative scoring method of glomerular injury, tubular degeneration and necrosis and interstitial inflammatory infiltration rated from 0 to 4 (0: none; 1: mild; 2: moderate; 3: marked; 4: severe) and the averages were taken from 10 non overlapping fields in each section at 400× magnification (Al-Obaidi *et al*., 2022).

Statistical analysis

The normality of the distribution was analyzed using the Shapiro-Wilk test. The test of homogeneity of variance was analyzed using Levene's test. Group differences were analyzed using one-way ANOVA followed by, if applicable, Dunnett's post-hoc test (each group vs control) and/or Tukey's test (for all pairwise comparisons). Results were expressed as mean ± SEM. ANOVA effect sizes (η^2) and 95% confidence intervals were provided when applicable. The criterion for statistical significance was set at $p < 0.05$.

RESULTS

Effect of EAC and therapeutic COE on renal function

When compared to the control group, the EAC group caused more serious damage to the kidneys. This group was the only one to show statistically significant increases in serum urea and creatinine compared with the control group, indicating that their kidneys have an impaired ability to filter blood. The therapeutic effect of the *Convolvulus oxyphyllus* extract resulted in a statistically significant decrease compared to untreated EAC mice ($p < 0.05$), but the levels tested remained above control levels. The COE-only group did not show statistically significant differences compared to the control levels, indicating that, at the tested dose, there was no intrinsic nephrotoxicity (Table 1).

Effect on serum electrolyte balance

The results presented in Table 1 exhibited that EAC-bearing mice showed marked electrolyte imbalances, as reflected by reduced sodium and calcium concentrations and elevated potassium and chloride levels compared with controls ($p < 0.05$). Partial restoration of electrolyte balance by COE treatment was evident, with a significant difference to the EAC group ($p < 0.05$). However, full restoration was not achieved.

Histopathological findings

Histological analyses of kidney sections from the control and COE-only groups showed intact, well-organised renal tubules, normal renal architecture, and intact glomeruli. In contrast, EAC-bearing mice exhibited glomerular shrinkage, disruption of renal architecture, interstitial cellular infiltration, and tubular degeneration. Semi-quantitative injury scoring showed that renal damage in the EAC group was significantly higher than in the control group ($p < 0.05$). Therapeutic COE treatment injury scores were significantly lower than those of the untreated EAC group ($p < 0.05$), but the improvement was less than that of the control group (Figure 1).

DISCUSSION

Renal impairment in female mice, as detected by increased serum urea and creatinine, lipid peroxidation, and decreased antioxidant enzyme activity, along with electrolyte imbalance and histo-pathological changes, is shown for the first time with the instillation of Ehrlich ascitic carcinoma (EAC). Recent studies also demonstrated renal dysfunction, renal cell apoptosis, and increased oxidative stress in the kidneys of EAC-treated mice (Tousson *et al*., 2024). The most significant positive effect of the treatment was the redox-modulating and renal-protective properties of the *Convolvulus oxyphyllus* extract.

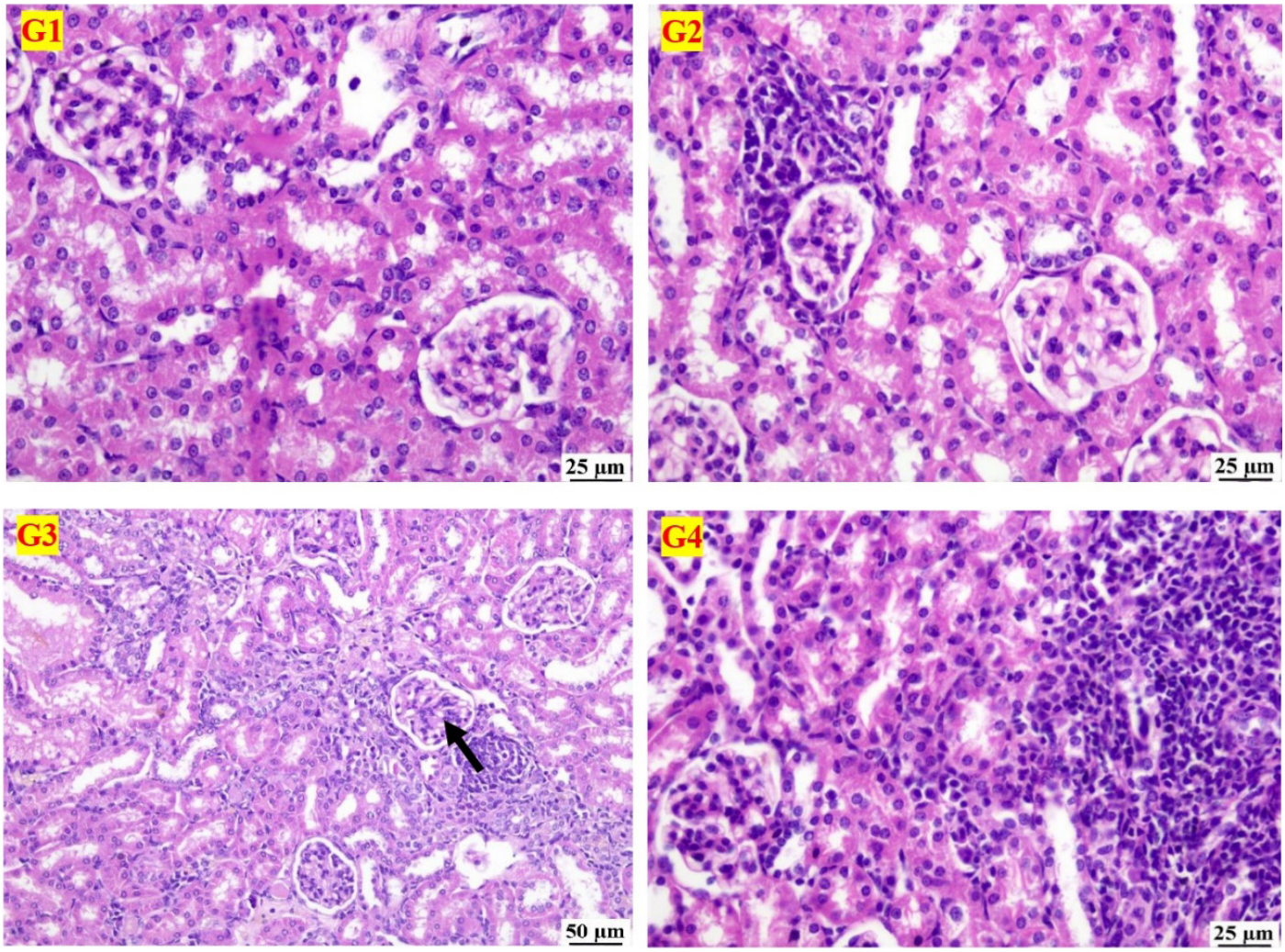

Figure 1: G1: Photomicrograph of kidney, Control group showing normal renal cortex (H & E). G2: Photomicrograph of kidney, COE groups showing mild interstitial inflammatory cells (H & E). G3: Photomicrograph of kidney, EAC group showing focal interstitial inflammatory cells infiltrate the renal cortex (arrow) (H & E). G4: Photomicrograph of kidney, EAC (1 days) + COE (14 days) group showing moderate interstitial nephritis (H & E).

The systemic and distant-organ effects of a tumour induce metabolic stress. The rapidly growing tumour cells overproduce reactive oxygen species (ROS), creating an oxidative imbalance within the body and causing distant organ dysfunction (El-Ghareeb *et al*., 2006).

Oxidative damage leads to lipid peroxidation, which disrupts membrane stability, ion transport, and mitochondrial function, in turn causing tubular damage and decreasing glomerular filtration (Alankooshi *et al*., 2023). This sequence of events is likely the explanation for the detection of increased serum urea and creatinine, and an electrolyte imbalance, in EAC-bearing mice. The bioactive compounds are known to alter the course of oxidative stress and enhance antioxidant defence mechanisms (Razooki *et al*., 2025; Hameed *et al*., 2025; Al-Hakeim *et al*., 2016). Although the parameters and markers of stress and function were not fully normalised to control values, the improvements in these parameters and stress markers likely indicate that COE preserves EAC-bearing renal function without fully reversing it. The continued presence of tumour burdens during treatment suggests that partial recovery is plausible. The histological findings complemented the biochemical findings (Abd El-Rahmana *et al*., 2024; Alankooshi *et al*., 2023).

The glomerular shrinkage, tubular degeneration, and interstitial infiltration caused by EAC are structural consequences of prolonged oxidative and metabolic stress 1,4,8. The COE treatment led to structural improvements and is consistent with the idea that improved redox homeostasis plays a protective role in renal architecture. Overall, these findings provide the first evidence for a mechanistic model of EAC-induced renal dysfunction, namely, oxidative stress-induced redox imbalance. The COE treatment improved this by subduing lipid peroxidation and increasing the body's endogenous antioxidant system (Alyasiri *et al*., 2025; Al-Khuzaay *et al*., 2024).

CONCLUSION

The therapeutic use of *Convolvulus oxyphyllus* extract improves EAC-induced renal dysfunction in female mice by primarily addressing oxidative stress and, to some extent, restoring the balance of redox. Improvements in biochemical, oxidative and histopathological parameters reinforce the relationship between tumours and redox imbalance, and subsequent renal injury. While the extract did not fully restore all parameters to normal, there was significant oxidative damage, indicating the need for further investigation to support the use of *Convolvulus oxyphyllus* in the treatment of tumour-related renal damage. More studies are required to clarify protective mechanisms on the molecular level.

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NOVELTY STATEMENT

Our study demonstrated that COE extract is effective against mice treated with EAC, based on the results obtained in kidney function, electrolytes, and kidney tissue.

AUTHOR'S CONTRIBUTION

Azhar Azher Al-Ankooshi, Fouad Razzaq Al-Burki, Zainab Alesawi: Study layout. Halah Flaeeih Hasan, Ahmed Flayyih Hasan: Methodology. Alaa A Akon, Hany M. El-Wahsh: Corresponding creator and manuscript enhancing, writing.

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Ethical approval

Experimental procedures comply with institutional guidelines and were approved by Biotechnology Research Center, Al-Nahrain University.

Generative AI and AI-assisted technology statement

The authors well known that that no artificial intelligence tools were used in the preparation of this article.

Conflict of interest

The authors pledge that there is no conflict of interest among themselves.

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