



Physiological Alterations in Hepatic Redox Homeostasis in Tumour-bearing Mice: Modulatory Effects of *Convolvulus oxyphyllus* Extract

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ABSTRACT

Background: Systemic metabolic load and redox imbalances are often associated with tumor burden and these conditions undoubtedly impair liver function. This research looked at how animals with ehrlich solid tumours (EST) altered their redox homeostasis and how *Convolvulus oxyphyllus* extract (COE) influenced these alterations.

Methods: Four groups of ten were randomly assigned to forty female swiss albino mice: Control, EST, EST COE (co-treatment) and EST → COE (Post-remedy). To learn more about the liver, we measured total protein, albumin and serum liver enzymes (ALT, AST and ALP). We examined hepatic redox markers, including catalase (CAT), superoxide dismutase (SOD) and malondialdehyde (MDA). To find structural alterations, a histological analysis was conducted.

Result: Mice with EST exhibited substantially reduced levels of albumin, total protein, SOD and CAT ($P < 0.05$) and considerably higher levels of ALT, AST, ALP and MDA compared with controls. This indicates an imbalance between the liver's capacity and redox homeostasis. Providing COE restored antioxidant enzyme activity and dramatically decreased oxidative stress indicators. Meanwhile, there were indications of improvement in blood chemistry indicators. Histological data, bolstered by biochemical effects, demonstrated reduced inflammation and hepatocyte degradation, particularly in the treated organisation. An extract of *Convolvulus oxyphyllus* changed how tumours affected liver function and redox homeostasis in mice. These results show that a redox-regulatory trait protects the liver from metabolic stress induced by cancer.

Key words: Antioxidant enzymes, *Convolvulus oxyphyllus*, Ehrlich solid tumour, Hepatic redox homeostasis, Liver function, Oxidative stress.

INTRODUCTION

The liver is the most important organ for controlling the body's metabolism. It controls how much energy is used, how proteins are made, how toxins are removed and how the balance between oxidation and reduction is kept. When things are normal, there is a delicate balance between the production of reactive oxygen species (ROS) and antioxidant defence systems that maintains hepatic redox homeostasis (Al-Saedi *et al.*, 2026). It's important to control the production of reactive oxygen species (ROS) to enable cells to communicate with one another. If this goes wrong for a long time, though, it could hurt cells and make them less stable. Tumour growth is now viewed as a systemic metabolic stressor rather than merely a localised growth phenomenon. Tumours that grow quickly need a lot of energy and biosynthesis, which can disrupt the metabolism of the organ they occupy, especially the liver (Porporato *et al.*, 2016; Klover *et al.*, 2004). In experimental models, including the ehrlich solid tumour (EST), changes in metabolic pathways and heightened mitochondrial activity lead to excessive production of reactive oxygen species (ROS), thereby inducing oxidative stress (Reuter *et al.*, 2010; Al-Obaidi *et al.*, 2022). Chronic oxidative stress may also exceed the frame's intrinsic antioxidant defences, leading to lipid peroxidation, faded enzyme activity and alterations in liver characteristic indicators (Giannini *et al.*,

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2005; Al-Dulimi *et al.*, 2025). Malondialdehyde (MDA) is not an unusual marker of cellular membrane damage because of oxidative stress. Superoxide dismutase (SOD) and catalase (CAT) are two important enzymes that protect cells from superoxide radicals and hydrogen peroxide. Changes in these markers can indicate how well the liver's redox balance functions under stress. If this stability is off, it can cause infection and liver tissue damage. People need to research medicinal flowers rich in phenolic and flavonoid compounds, as these compounds can help maintain cellular balance and manage oxidative stress (Tousson *et al.*, 2024; Mohammed *et al.*, 2025). The secondary metabolites within the *Convolvulus* genus are recognised for their anti-inflammatory and antioxidant properties. We lack sufficient knowledge of how *Convolvulus oxyphyllus* alters the liver's redox imbalance and the specific mechanisms underlying its tumour-promoting effects. This study aims to analyse changes in redox homeostasis in mice with EST and to evaluate the impact of *Convolvulus oxyphyllus* extract on liver dysfunction associated with tumours, using biochemical and histological analyses.

MATERIALS AND METHODS

Plant material and authentication

Aerial parts (leaves and stems) of *Convolvulus oxyphyllus* were collected from Basiyah District, Al-Muthanna Desert, Al-Muthanna Governorate, Iraq, in February 2023. The plant material was identified and authenticated by a qualified botanist using standard taxonomic keys.

Animals used in experiments

Forty female Swiss albino mice weighing 20-22 grams were purchased from [National Cancer Institute-Cairo University-Egypt]. The animals were housed under standard laboratory conditions, including a 12-hour light/dark cycle at 22±2°C and were allowed unlimited access to food and water. The animals were acclimated for a week before the experiment.

Design of experiments

Four groups of mice (n = 10 per group) were randomly assigned:

- **Group I (Control):** Just the car was received.
- **Group II (EST):** given the vehicle and injected with Ehrlich tumour cells (Kamaraj *et al.*, 2025).
- **Group III (EST + COE, co-treatment):** COE was administered for 14 days beginning on the day of tumour inoculation.
- **Group IV (EST → COE, post-treatment):** COE is administered for 14 days after the tumour has been allowed to develop for 7 days.

Identifying and administering the appropriate dosage

The COE dosage (15 mg/kg body weight/day) was consistent with OECD standards for acute oral toxicity and was based on previous research. A tube was used to give

the extract orally after it was freshly reconstituted in distilled water each day to a final dosage volume of 10 mL/kg.

Ehrlich solid tumour (EST) induction

Serial intraperitoneal passages were used to preserve Ehrlich tumour cells, which were obtained from the National Cancer Institute in Cairo, Egypt. Using trypan blue exclusion, the number of viable cells was determined. A subcutaneous injection of $2.5-3.0 \times 10^6$ viable cells suspended in 0.2 mL of phosphate-buffered saline (PBS) was administered to the left thigh of each mouse.

Gathering samples of tissue and blood

The rats were given an intraperitoneal injection of sodium pentobarbital to induce anaesthesia at the conclusion of the experiment. Samples of blood were drawn from the inferior vena cava into non-heparinised tubes and the serum was separated by centrifugation. After being removed and cleaned in ice-cold saline, liver tissues were examined histologically and biochemically.

Biochemical assessment

We used commercial diagnostic kits to measure blood levels of alkaline phosphatase (ALP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) according to the reitman-frankel method and the manufacturer's instructions. Using a spectrophotometer, standard methods were used to measure serum albumin and total protein.

Hepatic redox parameter assessment

Before centrifuging the liver tissues for 15 minutes at 4°C, we mixed them with ice-cold phosphate-buffered saline (pH 7.4). Tests were conducted using the supernatant.

The thiobarbituric acid reactive substances (TBARS) test was used to measure the amount of malondialdehyde (MDA) that was present. We measured superoxide dismutase (SOD) activity using the misra and fridovich approach. The Aebi method was used to measure catalase (CAT) activity. The protein content of liver homogenates was determined using the Bradford technique. We measured enzyme activity in milligrams of protein.

Examination of histopathology

The liver tissues were washed, dried and embedded in paraffin after being stored for 24 to 48 hours in 10% neutral buffered formalin. For microscopic examination, 5 µm sections were cut using a rotary microtome and then stained with hematoxylin and eosin (H and E) (Alankooshi *et al.*, 2023; Al-Hakeim *et al.*, 2016).

Statistical evaluation

Every data point is shown as mean±SEM. IBM Corp., Armonk, NY, USA's SPSS software (Version 26.0) was used to perform statistical analyses. After evaluating group differences using one-way analysis of variance (ANOVA), Tukey's post hoc multiple-comparisons test was used.

The threshold for statistical significance was set at a two-tailed P value of 0.05 or less.

Statement of ethics

Ethical approval was obtained under the consent obtained from Biotechnology Research Center/Al-Nahrain University.

RESULTS AND DISCUSSION

EST-induced hepatic damage

EST-caused liver injury

Blood levels of albumin and total protein dramatically dropped ($P < 0.05$). In contrast, blood activities of ALT, AST and ALP significantly rose when EST and self-treated EST were compared to control mice (Table 1). However, compared to the EST and self-treated EST groups, the COE-treated Co-treated (COE+EST) and post-treated (EST+COE) mice exhibited a significant decrease in ALT, AST and ALP levels and a significant increase in albumin and t-protein levels; the ameliorated group was more noticeable in the post-treated group (Table 1).

Activity of antioxidant enzymes

When EST and self-treated EST liver homogenates were compared to control mice, MDA levels were significantly higher and GSH, SOD and CAT activities were significantly lower (Table 2). However, comparing the EST+COE groups with the EST and self-treated EST groups showed substantial ($P < 0.05$) reductions in MDA and significant ($P < 0.05$) increases in SOD; the post-treated group showed a more pronounced ameliorative effect (Table 2).

Liver histopathology

In the liver tissues of COE groups of animals, the histological changes from the control group revealed hepatocytes with

eosinophilic cytoplasm, conspicuous round nuclei and a fine arrangement of Kupffer cells with a few spaced hepatic sinusoids between the hepatic cords (Fig 1 G1, G2). Additionally, COE showed significant tissue damage, including hepatic cord degeneration and noticeable inflammatory cells in liver tissues from EST-bearing mice and self-treated EST, along with pyknotic nuclei suggesting apoptosis, moderate fibrosis and widespread hepatocyte necrosis (Fig 1 G3). When EST mice were co-treated with COE, their liver sections showed mild damage and a noticeable recovery in all hepatocyte alterations (Fig 1 G4).

An event that causes things to grow. Tumour burden significantly affects the function of host organs, especially those involved in metabolism, such as the liver (Ayala *et al.*, 2014; Ighodaro *et al.*, 2018; Obaid *et al.*, 2025). The liver is very important for maintaining the body's metabolism, removing toxins and regulating redox. As a result, tumours place significant strain on the body's metabolism (Birben *et al.*, 2012). The current study found that mice with EST had clear biochemical and histological signs of liver problems. The blood had more ALT, AST and ALP, but less albumin and total protein. Because of these changes, the membranes of liver cells are less stable and the liver isn't producing as many proteins as it should. This makes sense with what we know about signs of liver damage (Razooki *et al.*, 2025; Ahmeda *et al.*, 2026).

Oxidative stress associated with tumours constitutes a significant molecular axis responsible for these alterations. When tumour cells grow quickly, their mitochondria are reprogrammed and their redox metabolism changes, leading to excessive reactive oxygen species (ROS) (Percie *et al.*, 2020; Abd El-Rahmana *et al.*, 2024). Reactive oxygen species (ROS) are essential for cellular signalling; however, excessive ROS can damage

Table 1: Variations in liver enzymes and functions in the studied groups.

	Group I	Group II	Group III	Group IV
AST (U/l)	42.8 [#] ±2.63	85.0 [*] ±2.43	70.8 [#] ±3.70	50.2 [#] ±0.86
ALT (U/l)	51.2 [#] ±1.63	89.8 [*] ±1.93	73.8 [#] ±1.99	62.6 [#] ±1.29
ALP (U/l)	47.7 [#] ±3.38	64.5 [*] ±2.53	41.3 [#] ±1.75	45.0 [#] ±4.99
T. proteins (g/dl)	7.8 [#] ±0.12	5.8 [*] ±0.17	7.0 [#] ±0.07	7.7 [#] ±0.20
Albumin (mg/dl)	3.56 [#] ±0.15	2.48 [*] ±0.15	3.12 [#] ±0.05	3.88 [#] ±0.19

The significance of modification was analyzed by one-way ANOVA. Values are expressed as means±SE. *and #Significant deviation from the EST group and the control, respectively at $p < 0.05$, while Control, Control group; COE: *Convolvulus oxyphyllus* extracts group; EST: Ehrlich solid tumor group; COE+EST: Co-treated group; EST+COE: Post-treated group; Self t. EST: Self-treated group.

Table 2: Effect of *Convolvulus oxyphyllus* extracts upon markers of oxidative stress in liver.

	Group I	Group II	Group III	Group IV
MDA (nmol/mg)	0.35 [#] ±0.02	1.94 [*] ±0.12	0.89 [#] ±0.04	0.42 [#] ±0.02
SOD (U/mg)	2.74 [#] ±0.20	1.12 [*] ±0.12	2.11 [#] ±0.18	2.25 [#] ±0.12

The one-way ANOVA was used to examine the significance of the difference. Means and SE are used to express values. Significant deviation from the control group and the EST group: *and # respectively at $p < 0.05$, while control, control group; COE: *Convolvulus oxyphyllus* extracts group; EST: Ehrlich solid tumor group; COE+EST: Co-treated group; EST+COE: Post-treated group; Self t. EST: Self-treated group.

proteins, nucleic acids and lipid membranes (Ohkawa *et al.*, 1979; Alankooshi *et al.*, 2023). The increased hepatic MDA levels in mice with EST confirm lipid peroxidation and membrane damage. The body's natural defences against free radicals are weakening because SOD and CAT levels have dropped significantly. Scientists agree that this difference between oxidative stress and antioxidant defence is a major reason why people with tumour organs fail (Alyasiri *et al.*, 2025). Histopathology studies support the idea that redox causes harm. The inflammation, liver cell damage, sinusoid disruption and necrotic changes observed in EST animals are analogous to the mitochondrial damage and cell death induced by reactive oxygen species (ROS). Oxidative stress has been shown to initiate pathways that lead to inflammation and fibrosis, worsening tissue damage beyond the initial oxidative injury (Bradford *et al.*, 1976; Al-Khuzayy *et al.*, 2024). The biochemical and histological results of this study support the idea that the main reason EST-bearing mice have liver problems is that their bodies are out of balance with oxidative stress. Natural bioactive compounds rich in flavonoids and phenolics have attracted greater attention as potential means to rebalance redox and oxidative stress associated with tumours. People know that some species of *Convolvulus* produce secondary metabolites that are

effective at fighting free radicals and reducing swelling (Percie *et al.*, 2020; Hameed *et al.*, 2025). The present study demonstrated that administration of *Convolvulus oxyphyllus* extract (COE) significantly reduced the elevated levels of malondialdehyde (MDA) and liver enzymes induced by EST. It also restored superoxide dismutase (SOD) and catalase (CAT) activity. The group that received treatment had a clearer path to recovery, suggesting that the redox-modulatory effect was more than just a way to stop the disease. Phenolic compounds safeguard cells by directly eliminating free radicals and modifying the functionality of antioxidant signalling pathways. The body's system for fighting free radicals depends on NRF2, which stands for nuclear factor (erythroid-derived 2)-like 2 (Al-Saeedi *et al.*, 2026). It controls the transcription of genes that encode enzymes that help cells eliminate toxins and protect them from damage. When NRF2 is activated, it restores redox balance, prevents lipid peroxidation and protects tissues from damage during pathological stress. This study did not immediately analyse NRF2 expression; however, the restoration of SOD and CAT activity to baseline levels post-COE treatment indicates that the frame's intrinsic antioxidant mechanisms were enhanced rather than merely exhibiting a chemical antioxidant effect (Sies *et al.*, 2020; Al-Obaidi *et al.*, 2022). Controlled changes in

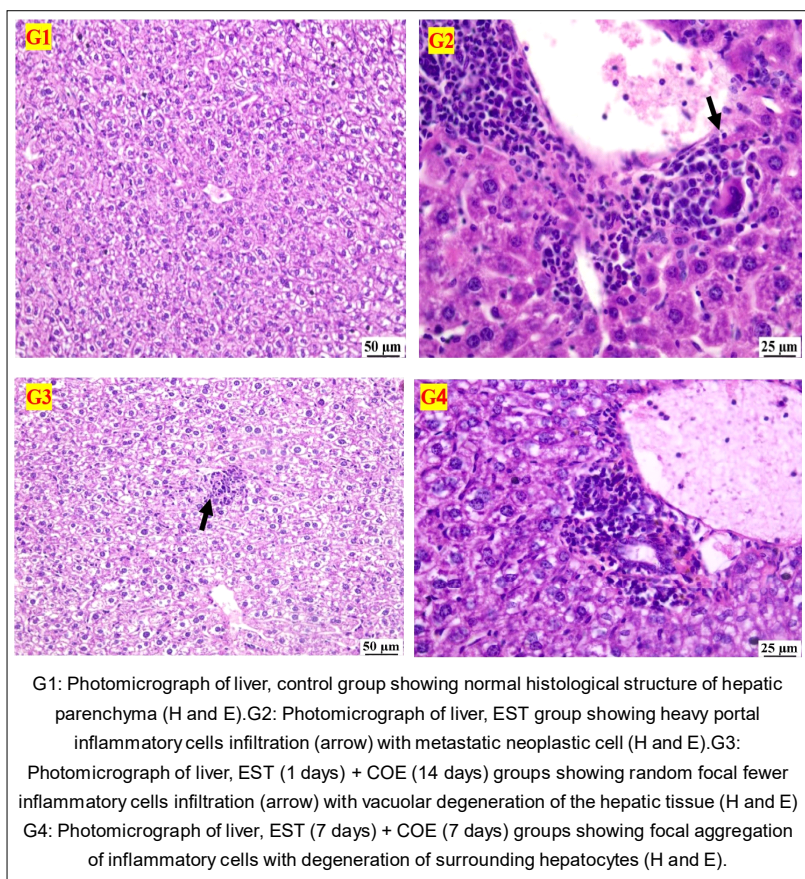


Fig 1: Liver histopathology.

oxidative stress are becoming a more likely option for cancer patients who have tried a lot of other treatments. Cancer cells need a very carefully controlled redox stability to keep growing without causing oxidative stress, which is bad. There are ways to restore the body's redox balance to normal that don't involve prolonging tumour survival, but they aren't easy. The results of this study support the idea that COE might also protect the liver by boosting its antioxidant defences and reducing the oxidative damage caused by the tumour burden (Reczek *et al.*, 2017; Hayes *et al.*, 2014; Ahmed *et al.*, 2025). The results show that tumour-induced oxidative stress is a major driver of liver problems in animals with EST. *Convolvulus oxyphyllus* extract safeguards the liver by regulating redox reactions. We should investigate the molecular mechanisms of antioxidant signalling pathways to understand better how these protective effects work and to develop COE as a more effective treatment for tumour-induced liver damage. One option is to look into NRF2 and the things it controls (Kashyap *et al.*, 2021; Zhang *et al.*, 2020; Al-Dulimi *et al.*, 2025).

CONCLUSION

The recent findings indicate that tumour burden is associated with significant physiological disturbances in hepatic redox homeostasis and functional integrity in mice. The initiation of ehrlich solid tumours led to oxidative imbalance, diminished antioxidant defence and alterations in critical biochemical indicators of liver function, accompanied by structural changes in the liver. The management of *Convolvulus oxyphyllus* extract alleviated tumour-related disruptions by reducing lipid peroxidation and restoring antioxidant enzyme activities, crucially leading to concurrent enhancements in biochemical and histological parameters. The more significant large outcomes observed in the post-treatment business indicate a regulatory effect under recognised tumour-induced metabolic stress. These results support the hepatoprotective and redox-regulatory properties of *Convolvulus oxyphyllus* extract in tumour-bearing mice. Further molecular-stage investigations are essential to elucidate the regulatory pathways that control this physiological modulation.

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Conflict of interest

No conflict of interest exists between the authors.

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