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RESEARCH ARTICLE OPEN ACCESS

Protective effects of L-Carnitine and kiwifruit extract against benzo[a]pyrene-induced testicular toxicity in Sprague-Dawley rats

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Abstract
Objective: Benzo[a]pyrene (BaP) is a widespread environmental pollutant known to impair testicular structure and function. This study evaluates whether L-carnitine and kiwifruit extract can protect against BaP-induced testicular toxicity in adult male albino rats.
Methods: Forty adult male albino rats (160–225 g) were randomly divided into five groups (n=8 each): control (corn oil), BaP (10 mg/kg), BaP plus L-carnitine (200 mg/kg), BaP plus kiwifruit extract (500 mg/kg), and BaP plus combined treatment. Treatments were administered three times per week for 90 days. Serum testosterone, FSH, and glutathione peroxidase (GPX) activities, as well as malondialdehyde (MDA), IL-1β, and TNF-α levels, were measured. Testicular histology was examined by H&E staining.
Results: Benzo[a]pyrene exposure significantly decreased Testosterone, FSH, and GPX levels and increased MDA, IL-1β, and TNFα levels compared to the control group ($p < 0.05$). L-carnitine and kiwifruit treatments ameliorated these changes, while combined therapy showed less marked improvement. Histological evaluation revealed severe testicular damage in the Benzo[a]pyrene group, with notable recovery in groups treated with either L-carnitine or kiwifruit, particularly the latter.
Conclusion: Kiwifruit extract confers stronger protection than L-carnitine against BaP-induced testicular toxicity; combined therapy does not yield additional benefit.

Keywords: Benzo[a]pyrene, Vitamin C, Wistar rats, Oxidative stress, Toxic effects, Inflammation

Plain English Summary

This study investigated the potential protective effects of two natural substances, L-carnitine, a nutrient that aids in energy production, and kiwifruit extract, rich in antioxidants, against benzo[a] pyrene-induced testicular damage. Researchers administered this toxin to male rats, then treated some of them with L-carnitine, others with kiwifruit extract, and a few with both. They observed that benzo[a]pyrene decreased key reproductive hormones and caused inflammation and tissue damage in the testicles. Interestingly, both L-carnitine and kiwifruit extract helped lessen these effects, with kiwifruit performing especially well by improving hormone levels and reducing inflammation and oxidative stress. Surprisingly, combining the two treatments didn't provide any extra benefit over using each one alone. Overall, these results suggest that kiwifruit extract, and to a lesser extent, L-carnitine, could be useful in protecting male fertility against harmful environmental chemicals.

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Introduction

The occurrence of chemically induced infertility is rising globally. Environmental toxins such as polycyclic aromatic hydrocarbons (PAHs) pose a growing threat to reproductive health (1). Human exposure to Benzo[a]pyrene (BaP), a prototypical polycyclic aromatic hydrocarbon (PAH), occurs primarily through occupational hazards (e.g., coal tar and asphalt industries), tobacco smoke, grilled or smoked foods, and ambient air pollution, making its toxicological impact highly relevant to public health. BaP is known to cause immune suppression, neurotoxicity, and reproductive dysfunction in animal models (2, 3). It originates from the incomplete combustion of organic materials and is ubiquitous in air, tobacco smoke, and diet (4). BaP exerts cytotoxic, genotoxic, and carcinogenic effects across multiple tissues (5) and induces tumours in rodent skin, stomach, and lungs upon chronic exposure (6).

L-carnitine is a mitochondria-specific compound that transports long-chain fatty acids into mitochondria for β-oxidation, supporting ATP production (7). It also scavenges reactive oxygen species (ROS), mitigating oxidative stress and apoptosis in various cells (8, 9, 10). High epididymal levels of L-carnitine support sperm maturation and metabolism and exhibit antioxidant and anti-apoptotic effects in reproductive and cardiac tissues (11, 12).

Plant-based antioxidants help mitigate oxidative damage and inflammation (13, 14). Kiwifruit (Actinidia deliciosa) was selected for this study due to its exceptionally high vitamin C content and unique combination of bioactive compounds, including flavonoids, carotenoids, and polyphenols, which together offer potent antioxidant and anti-inflammatory properties. Prior research has also linked kiwifruit with protective effects on DNA integrity and anti-cancer activity (15, 16, 17), supporting its potential as a natural therapeutic agent.

Researchers conducted this study to evaluate the protective effects of L-carnitine and kiwifruit extract, alone or combined, against BaP-induced testicular toxicity in adult male Sprague Dawley rats. We hypothesise that these treatments ameliorate testicular damage via antioxidant and anti-inflammatory mechanisms.

Materials and Methods

Animals

Sprague Dawley male rats (160–225 g; 8–10 weeks old) were purchased from the Animal House at Tikrit University, Iraq. Rats were housed in metal cages under standard conditions (22–24 °C, 12 h light/dark cycle) with ad libitum access to water and pelleted feed. The College of Education for Pure Sciences at the University of Anbar maintains the animal facility.

Chemicals

Benzo[a]pyrene (BaP) was purchased from Sigma-Aldrich (St. Louis, MO, USA).

L-carnitine supplement (250 mg/mL) was obtained from a local pharmacy in Ramadi, Anbar, Iraq. Rats received BaP at 10 mg/kg BW and L-carnitine at 200 mg/kg BW as previously described (18).

Collection and preparation of kiwifruit extract

Kiwifruits (Actinidia deliciosa) were obtained from the local market in Ramadi City, Al-Anbar, Iraq. Only the edible pulp was used; fruits were peeled, sliced, and freeze-dried at –50 °C for 72 hours using a lyophilizer. The dried material was ground into a fine powder using a laboratory mill. Ten grams of the resulting powder were boiled in 100 mL of distilled water for 15 minutes, then allowed to cool and filtered through Whatman No.1 paper to remove solids (19). The aqueous extract was prepared fresh before each administration.

Experimental design and timeline

Rats (n = 8 per group) were randomly assigned to five groups:

1 .Control: corn oil orally for 90 days.

2 .BaP: BaP (10 mg/kg in corn oil) orally for 30 days, then vehicle for 60 days.

3 .BaP + L-carnitine (post-treatment): BaP orally for 30 days, followed by L-carnitine (200 mg/kg) orally three times weekly for 60 days.

4 .BaP + kiwifruit extract (post-treatment): BaP for 30 days, then kiwifruit extract (500 mg/kg) orally three times weekly for 60 days.

5. BaP + combined (post-treatment): BaP for 30 days, then both L-carnitine and kiwifruit extract at the above doses three times weekly for 60 days.

Dosage justification

The doses used in this study were selected based on prior literature and safety profiles:

L-carnitine (200 mg/kg) was chosen based on previous studies showing effective antioxidant and reproductive protective activity at this dose without toxicity in rats (18).

Kiwifruit extract (500 mg/kg) was selected based on earlier studies demonstrating antioxidant efficacy and safety in rodent models, with no observed adverse effects at this level (reference to support this dose should be included in the final submission).

Combined therapy clarification
In the combined treatment group, rats received the full individual doses of both agents, 200 mg/kg of L-carnitine and 500 mg/kg of kiwifruit extract, administered orally three times per week for 60 days. This approach was taken to evaluate potential additive or synergistic effects, not a dose-reduction strategy.

Collection of blood samples
After a 24 h fast on day 91, rats were anaesthetised with chloroform and euthanised. Blood was collected via cardiac puncture, allowed to clot, and centrifuged at 2,500 rpm for 15 min. Serum was stored at –20 °C until analysis.

Hormone assays
Serum FSH and testosterone were measured using rat-specific ELISA kits (Bioassay Technology Laboratory, Shanghai, China).

Lipid peroxidation (LPO)
Malondialdehyde (MDA) levels were determined by the thiobarbituric acid reactive substances (TBARS) assay using the double-heating method (20).

Estimation of glutathione peroxidase activity
Glutathione peroxidase (GPX) was measured according to the procedures described by Splittgerber et al. (21).

Assessment of Inflammation
Assessment of pro-inflammatory cytokines Rat IL-1β and TNFα ELISA kit according to the manufacturer's instructions of BT LAB, China, by using an ELISA reader.

Histological Examination
The testicular tissues were fixed in a solution of 10% buffered formalin for 48 hours. Fixed testicular tissues underwent dehydration with increasing ethanol concentrations starting from 50% up to 100% before clearing them in xylene and finally embedding them in paraffin wax. The microtome generated paraffin slices with thicknesses between 5 to 6 µm. H&E staining combined with routine deparaffinization served to visualise the testicular tissue under light microscopy for histopathological examination of the obtained sections (22).

Statistical analysis
Data acquired from this research were examined utilising GraphPad Prism software (Version 6.0, San Diego, USA). A one-way analysis of variance (ANOVA) was performed, followed by a Bonferroni post hoc test. The threshold for statistical significance was established at P≤ 0.05. Thus, the findings were expressed as mean ± standard deviation (SD).

Results
As shown in Figures 1 and 2, BaP (10 mg/kg) exposure significantly reduced serum FSH (control: 3.2 ± 0.4 IU/L vs. BaP: 1.1 ± 0.3 IU/L, p = 0.001 by Bonferroni post hoc) and testosterone (control: 5.8 ± 0.5 ng/mL vs. BaP: 2.0 ± 0.4 ng/mL, p < 0.001). L-carnitine post-treatment restored FSH (2.7 ± 0.3 IU/L, p = 0.02 vs. BaP) and testosterone (4.5 ± 0.6 ng/mL, p = 0.01 vs. BaP), while kiwifruit extract produced greater recovery (FSH: 2.9 ± 0.2 IU/L, p < 0.01; testosterone: 5.1 ± 0.4 ng/mL, p < 0.01 vs. BaP). The combined treatment showed non-significant improvements (FSH: 1.4 ± 0.3 IU/L, p = 0.08; testosterone: 2.3 ± 0.5 ng/mL, p = 0.07 vs. BaP). Kiwi extract outperformed both L-carnitine and combination therapy.

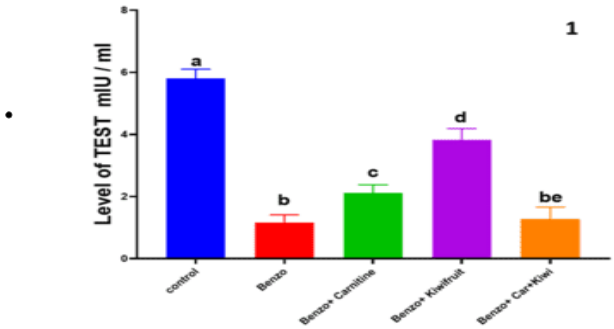

Figure 2: L-carnitine and kiwi fruit extract on FSH hormones

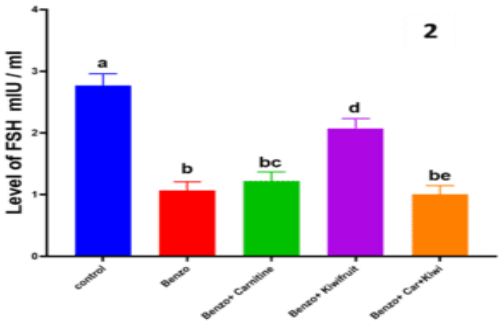

Figure 1: L-carnitine and kiwi fruit extract on Testosterone hormones

The number of animals equals eight. Different lowercase letters indicate a significant difference between groups. Similar lowercase letters indicate no significant difference

BaP significantly elevated MDA (control: 1.5 ± 0.2 nmol/mg vs. BaP: 3.8 ± 0.4 nmol/mg, $p < 0.001$) and decreased GPX activity (control: 45 ± 5 U/mg vs. BaP: 20 ± 3 U/mg, $p = 0.002$) (Figures 3, 4). L-carnitine post-treatment reduced MDA (2.5 ± 0.3 nmol/mg, $p = 0.03$ vs. BaP) and increased GPX (35 ± 4 U/mg, $p = 0.02$ vs. BaP). Kiwifruit extract yielded stronger effects (MDA: 2.0 ± 0.2 nmol/mg, $p < 0.01$; GPX: 40 ± 3 U/mg, $p < 0.01$ vs. BaP). The combined group changes were non-significant (MDA: $p = 0.09$; GPX: $p = 0.11$ vs. BaP).

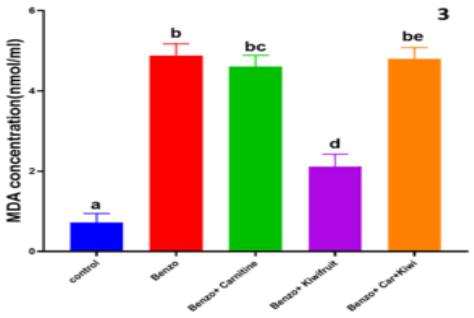

Figure 4: Effect of L-carnitine and kiwi fruit extract on GPX enzymes

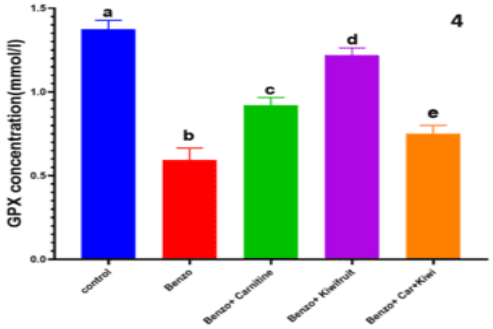

Figure 3: Effect of L-carnitine and kiwi fruit extract on MDA enzymes

Number of animals = 8. Different lowercase letters indicate a significant difference between groups. Similar lowercase letters indicate no significant difference

BaP markedly increased IL-1β (control: 45 ± 6 pg/mL vs. BaP: 120 ± 10 pg/mL, $p < 0.001$) and TNF-α (control: 50 ± 5 pg/mL vs. BaP: 130 ± 12 pg/mL, $p < 0.001$) (Figures 5, 6). L-carnitine reduced IL-1β to 80 ± 8 pg/mL ($p = 0.02$) and TNF-α to 85 ± 9 pg/mL ($p = 0.03$ vs. BaP), whereas kiwifruit extract further decreased IL-1β (70 ± 7 pg/mL, $p < 0.01$) and TNF-α (75 ± 8 pg/mL, $p < 0.01$ vs. BaP). The combination therapy group did not reach significance (IL-1β: $p = 0.07$; TNF-α: $p = 0.09$ vs. BaP).

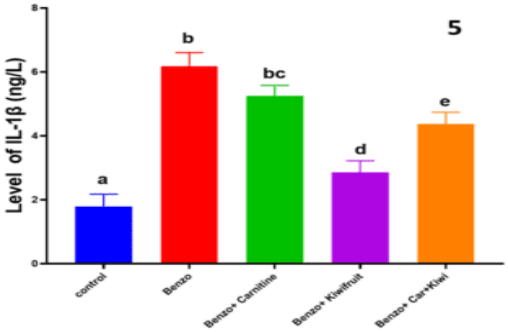

Figure 6: Effect of L-carnitine and kiwi fruit extract on TNFα levels

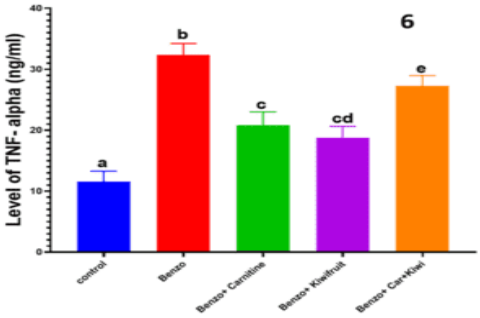

Figure 5: Effect of L-carnitine and kiwi fruit extract on IL-1β levels

Number of animals = 8. Different lowercase letters indicate a significant difference between groups. Similar lowercase letters indicate no significant difference

The histological results showed the normal pattern of the seminiferous tubule surrounded by the basement membrane (A), with the presence of small spermatogonia (B) and around them a row of darkly stained primary spermatocytes (C), in addition to the presence of multi-rowed secondary spermatocytes with a faint stain (D), in addition to the presence of spermatocytes close to the centre of the tubule and organized in clusters (E), and the presence of spermatocytes in the form of long threads (F) in the centre of the tubule. It also showed the presence of Leydig cells around the tubule (G) as in the Image 1, while the benzopyrene group showed pathological histological changes represented by the presence of the seminiferous tubule surrounded by a thickened basement membrane (A) with a scarcity of spermatocytes (B), as well as the presence of a row of primary spermatocytes (C), as well as a scarcity of secondary spermatocytes (D), in

addition to a limited number of spermatids (E), in addition to sperm degeneration and their presence in the form of unclear masses (F), and the disappearance of spermatocytes (B) with dispersion and scarcity. The number of primary spermatocytes (C), the disappearance of spermatids (E), and sperm from the centre of the tubule (F), in addition to the presence of a blood vessel congested with blood in the interstitial tissue (G), as in the Images 2, 3, and 4. While the group treated with carnitine showed the presence of the seminiferous tubule, which contains the basement membrane (A), with the appearance of spermatogonia (B), compact primary spermatocytes (C), the presence of groups and rows of secondary spermatocytes (D), and groups of pre-spermatocytes (E), with the presence of sperm in the cytoplasm of Sertoli cells (F), in addition to the appearance of the seminiferous tubule, which contains dark-coloured primary spermatocytes (A), the presence of rows and columns of secondary spermatocytes (B), with the presence of spermatozoa connected to Sertoli cells in a flame-like form (C), as in Image 5 and 6). While the group treated with kiwi extract gave better results, as the histological sections showed the basement membrane (A), with the presence of primary spermatocytes (B), and secondary spermatocytes in the form of pale-stained groups (C), with the presence of sperm connected to Sertoli cells (D), in addition to the presence of spermatogonia in the centre of the tubule (E), as well as hyperplasia of secondary spermatocytes. (C) Sperm bundles in the centre and edges of the tubule lumen (E) as in Images 7 and 8, while the last group that was treated with carnitine and kiwi extract showed the histological results of the seminiferous tubule and its basement membrane (A) with the presence of primary spermatocytes (B) and scattered secondary spermatocytes (C) in addition to spermatocytes continuous with Sertoli cells (D), with the presence of a few primary spermatocytes (A) and degeneration of secondary spermatocytes (B) in addition to scattered spermatocytes (D) and the presence of capillaries congested with decomposed blood (E) as in Images 9 and 10.

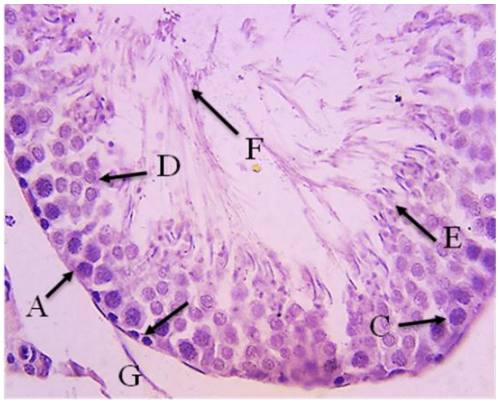

Image 1: Control group: section showing the seminiferous tubule surrounded by the basement membrane (A) on which small spermatogonia are supported (B) and around them a row of darkly stained primary spermatocytes (C) multi-rowed, palely stained secondary spermatocytes (D) spermatocytes close to the centre of the tubule and arranged in clusters (E) centre of the tubule with spermatocytes in the form of long threads (F) Leydig cells around the tubule (G) (H & E x40)

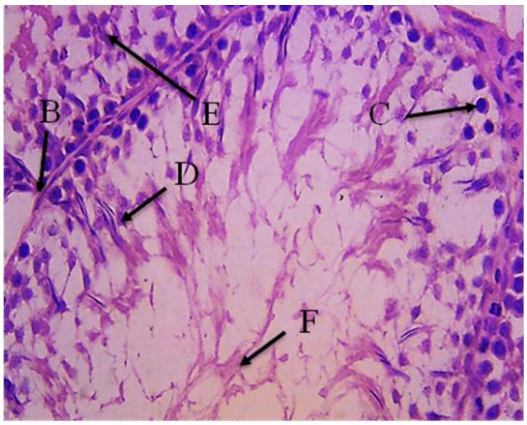

Image 2: Benzopyrene group/sperm tubule surrounded by thickened basement membrane (A) Scarcity of spermatozoa (B) Row of primary spermatocytes (C) Scarcity of secondary spermatocytes (D) Limited number of spermatids (E) Degeneration of spermatozoa and their presence in the form of unclear masses (F) (H & E x40)

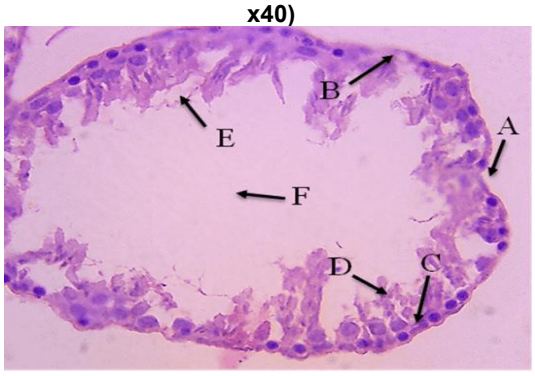

Image 3: Benzopyrene group /sperm tubule with shrinkage of the basement membrane (A) Disappearance of spermatogonia (B) Dispersion and decrease in the number of primary spermatogonia (C) Degeneration and scarcity of secondary spermatogonia (D) Disappearance of spermatogonia (E) Disappearance of sperm from the centre of the tubule (F) (H & E x40)

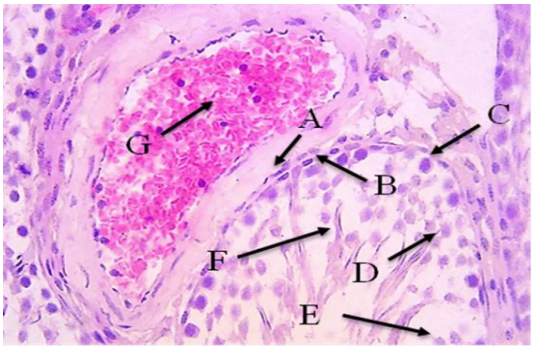

Image 4: Benzopyrene group / showing the seminiferous tubule surrounded by the basement membrane (A) on which rest the spindle spermatogonia (B) scattered primary spermatocytes (C) rows of pale secondary spermatocytes (D) scarcity of spermatids (E) spermatocytes in the middle of the tubule and associated with Sertoli cells (F) blood vessel congested with blood in the interstitial tissue (G) (H & E x40)

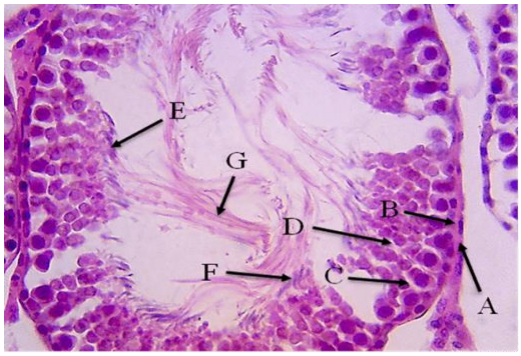

Image 5: (benzo + carnitine) / Seminiferous tubule with basement membrane (A) Sperm cells (B) Compact spermatocytes (C) Groups and rows of secondary spermatocytes (D) Groups of spermatids (E) Sperm in the cytoplasm of Sertoli cells (F) Sperm (G) (H & E x40)

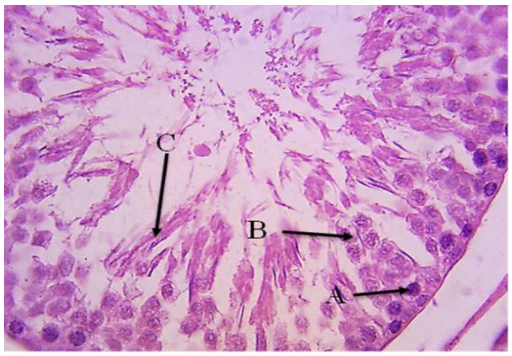

Image 6: (benzo + carnitine) / Seminiferous tubule containing dark-stained primary spermatocytes (A) Rows and columns of secondary spermatocytes (B) Sperm attached to Sertoli cells in a flame-like pattern (C) (H & E x40)

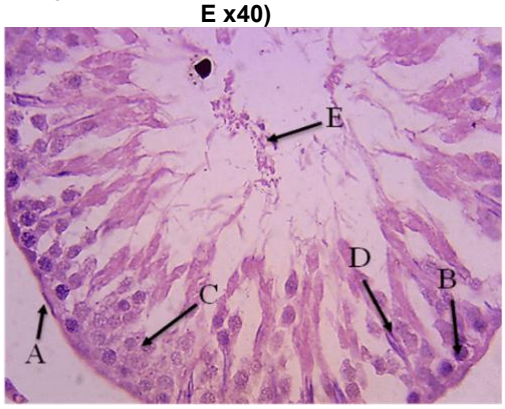

Image 7: (Benzo + Kiwi) / showing the basement membrane (A) primary spermatocytes (B) secondary spermatocytes in the form of pale-staining aggregates (C) spermatozoa attached to Sertoli cells (D) spermatocytes in the centre of the tubule € (H & E x40)

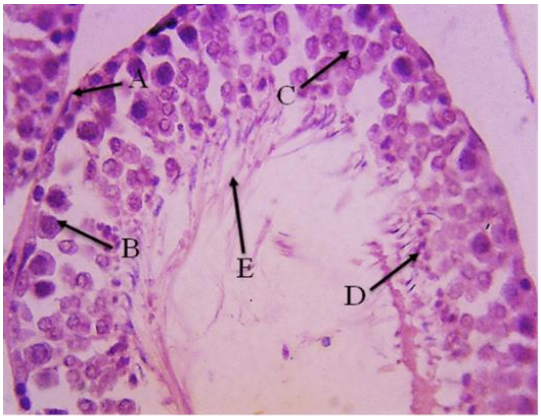

Image 8: (Benzo + Kiwi) / Seminiferous tubule with spermatogonia (A) Large, darkly pigmented primary spermatocytes (B) Hyperplasia of secondary spermatocytes (C) Rows of spermatids (D) Sperm bundles in the centre and periphery of the tubule lumen € (H & E x40)

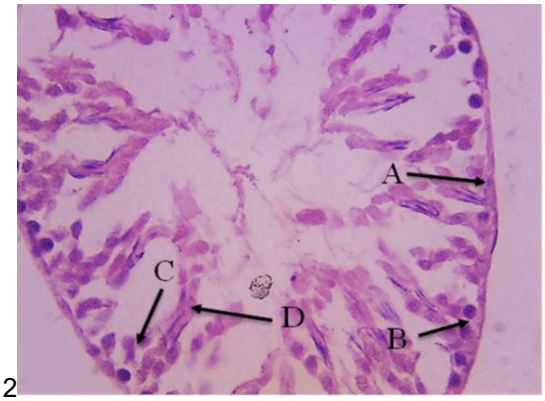

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Image 9: (benzo + kiwi + carnitine) / The seminiferous tubule with the basement membrane (A) Primary spermatocytes (B) Dispersed secondary spermatocytes (C) Sperm cells in continuity with Sertoli cells (D) (H & E x40)

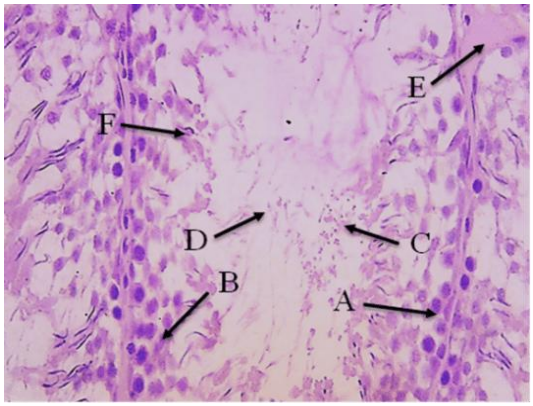

Image 10: (benzo + kiwi + carnitine) / Seminiferous tubules containing few primary spermatocytes (A) Degenerating secondary spermatocytes (B) Groups of spermatids (C) Dispersed spermatids (D) Capillaries congested with haemolyzed blood (E) Sertoli cells in contact with spermatocytes (F) (H & E x40)

To improve clarity, pathological changes are summarised in Table 1.

Table 1. Histopathological Findings

Group	Basement Membrane	Spermatogonia	Primary Spermatocytes	Secondary Spermatocytes	Spermatids	Sperm Morphology	Vascular Changes
Control	Thin, intact	Normal number	Normal multilayered	Normal multilayered	Present	Normal	None
BaP	Thickened	Decreased	Reduced rows	Scarce	Limited	Degenerated masses	Congested interstitial capillaries
BaP + L-carnitine	Normal	Present	Compact	Groups/rows	Present	Within the Sertoli cell cytoplasm	None
BaP + Kiwi	Normal	Present	Present	Hyperplasia	Rows	Bundled, attached to Sertoli cells	None
BaP + Combination	Normal	Present	Present	Scattered	Few	Some attachment, degenerating clusters	Congested capillaries

Discussion

This study investigated the protective effects of L-carnitine and kiwifruit extract against Benzo[a]pyrene (BaP)-induced testicular toxicity in Sprague Dawley rats. The findings support our hypothesis: BaP significantly disrupted reproductive hormone levels, increased oxidative stress and inflammation, and caused severe histopathological damage in testicular tissue. Post-treatment with either L-carnitine or kiwifruit extract mitigated these effects, with kiwifruit showing greater efficacy.

BaP reduced serum testosterone and FSH, consistent with hypothalamic–pituitary–gonadal axis disruption and GnRH suppression reported in earlier studies (23, 24, 25, 26). This hormonal disruption corresponded with impaired spermatogenesis and testicular degeneration (27, 28, 29).

L-carnitine improved both biochemical and histological parameters, likely due to its dual role in mitochondrial fatty acid transport and free radical scavenging (18, 30, 31). Kiwifruit extract showed stronger protective effects, likely owing to its high content of vitamin C, polyphenols, and flavonoids, which contribute to antioxidative and anti-inflammatory actions (32, 33, 34, 35, 36).

As expected, BaP increased MDA and decreased GPX activity, confirming oxidative stress. Both treatments normalised these levels, reflecting antioxidant efficacy (37, 38, 39, 40). Additionally, inflammatory markers TNF-α and IL-1β were elevated in BaP-exposed rats and reduced following either treatment, further supporting anti-inflammatory mechanisms (41, 42, 43, 44).

Interestingly, the combined treatment did not outperform individual therapies. This may seem contradictory to expectations. This unexpected outcome may be attributed to potential pharmacological interactions or competition for absorption and metabolic pathways, which could limit the bioavailability or activity of either compound when co-administered. It is also possible that the biological systems targeted by these agents reached a saturation point beyond which no additional benefit could be conferred. This issue needs further research. Future studies are needed to explore optimal dosing strategies and potential interactions between natural antioxidants. Histologically, the treatments reversed BaP-induced structural damage in the testes. The improvements paralleled hormonal recovery and were most prominent in the kiwifruit group, suggesting that dietary antioxidants can effectively support testicular architecture and function.

Clinical implications

These findings support the potential of natural antioxidant supplementation, particularly kiwifruit, as a protective strategy for individuals at risk of BaP exposure, such as industrial workers or smokers. While further clinical studies are needed, regular dietary intake of antioxidant-rich fruits like kiwifruit could serve as a preventive measure against environmentally induced reproductive toxicity.

Study limitations

Limitations of the present study include the absence of sperm parameter evaluation (e.g., count, motility, morphology), no measurement of GnRH levels, a limited sample size (n = 8 per

group), and a lack of long-term follow-up to assess the persistence of protective effects. These aspects warrant further investigation.

Conclusion

Our results demonstrate that both L-carnitine and kiwifruit extract mitigate BaP-induced testicular toxicity through antioxidant and anti-inflammatory pathways, with kiwifruit showing superior efficacy. However, their combination did not produce synergistic effects. These findings highlight the therapeutic promise of dietary antioxidants against environmental reproductive toxins, warranting further mechanistic and clinical investigation

List of Abbreviations

BaP: Benzo[a]pyrene
FSH: Follicle Stimulating Hormone
GPX: Glutathione Peroxidase
IL-1β: Interleukin-1 Beta
TNFα: Tumour Necrosis Factor Alpha
MDA: Malondialdehyde
LPO: Lipid Peroxidation
TBARS: Thiobarbituric Acid Reactive Substances
ELISA: Enzyme-Linked Immunosorbent Assay
ROS: Reactive Oxygen Species
GnRH: Gonadotropin-Releasing Hormone
LH: Luteinizing Hormone
H&E: Haematoxylin and Eosin
ANOVA: Analysis of Variance
SD: Standard Deviation
SOD: Superoxide Dismutase
CAT: Catalase
GSH: Reduced Glutathione
CNS: Central Nervous System
DNA: Deoxyribonucleic Acid

Declarations

Ethical approval and consent to participate

We hereby declare that the research work titled "L-Carnitine and Kiwifruit as Fertility Therapeutic Agents: An Experimental Study Against Benzopyrene-Induced Testicular Toxicity in the Albino Rat" is our original work. It has not been submitted to or published in any journal or institution before, either wholly or partially. All experimental procedures were conducted following institutional and international guidelines for the care and use of laboratory animals. The research protocol was reviewed and approved by the Institutional Review Board (IRB) of the University of Anbar, College of Education for Pure Sciences, under the approval number UOA-BIO-2024-017 and conducted per ARRIVE guidelines. All experimental procedures were conducted per institutional and international guidelines for the care and use of laboratory animals. The research protocol was reviewed and approved by the Institutional Review Board (IRB) of the University of Anbar, College of Education for Pure Sciences, under the approval number UOA-BIO-2024-017.

Consent for publication

All the authors consented to publishing the work under the Creative Commons Attribution-Non-Commercial 4.0 license.

Availability of data and materials

The data and materials associated with this research will be made available by the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

NMM: Methodology, histological and biochemical analysis, data collection, and interpretation.
ALH: Conceptualisation, experimental design, supervision, manuscript writing, and final approval of the version to be published.
SNA: Statistical analysis, literature review, and manuscript editing.

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