



Differential Cardio-Hepatic and Serum Mineral Responses to Orange-Peel, Date-Seed, and Common-Bean-Seed Extracts During Chronic Aspirin Exposure in Female Rats

Dalal Turki Shattnan Al Gabri¹, Mohammed Mahdi Yaseen²

¹Ministry of Education, General Directorate of Education in Al-Qadisiyah, Iraq Correspondence Email: dalal.turki@qu.edu.iq,
<https://orcid.org/0009-0002-8238-8418>,

²Department of Public Health, College of Veterinary Medicine, University of Al-Qadisiyah, Al-Diwaniyah City, Iraq,
mohammed.yaseen@qu.edu.iq, <https://orcid.org/0000-0003-4285-5739>

ARTICLE INFO

Article history:

Received 11 Apr. 2026

Revised 22 May 2026

Accepted 25 May 2026

Published 01 Jun. 2026

Keywords:

aspirin; *Citrus sinensis*; *Phoenix dactylifera*; *Phaseolus vulgaris*; cardiac biomarkers; liver enzymes; serum electrolytes

ABSTRACT

Background: Chronic aspirin exposure can alter biochemical indices across several organ systems, whereas plant-derived phenolic compounds may modify these responses. **Objective:** The study evaluated the effects of hot ethanolic extracts of orange peel (*Citrus sinensis*), date seeds (*Phoenix dactylifera*), and common-bean seeds (*Phaseolus vulgaris*) on cardiac biomarkers, hepatic enzymes, and serum minerals in female rats receiving aspirin. **Methods:** Twenty-five female albino rats (approximately 250 g) were allocated to five groups (n=5): control (C), aspirin 20 mg/kg (A), orange-peel extract 150 mg/kg plus aspirin (B), date-seed extract 150 mg/kg plus aspirin (T), and bean-seed extract 150 mg/kg plus aspirin (F). Treatments were administered orally once daily for 30 days. Serum myoglobin, troponin I, CK-MB, ALT, AST, ALP, potassium, chloride, sodium, and calcium were quantified. Data are expressed as mean $\pm$ SD and group differences were evaluated by one-way ANOVA with Fisher's least significant difference criterion at $P < 0.05$. **Results:** Date-seed treatment produced the lowest CK-MB value (0.46 ± 0.15 ng/mL) and maintained myoglobin at 0.72 ± 0.09 ng/mL, both sharing the lowest significance class with control. Orange-peel plus aspirin showed the highest troponin I (0.026 ± 0.006 ng/mL) and CK-MB (0.90 ± 0.08 ng/mL). Hepatic responses differed sharply from the cardiac pattern: bean-seed plus aspirin produced the highest ALT (486.4 ± 42.7 U/L) and AST (526.6 ± 35.8 U/L), whereas aspirin alone and orange-peel plus aspirin had the lowest aminotransferase activities. ALP was lowest in control (53.332 ± 3.11 U/L) and highest in aspirin and orange-peel groups. Bean-seed treatment also produced the highest chloride (110.2 ± 0.37 mmol/L) and sodium (155.6 ± 2.50 mmol/L), while date-seed and bean-seed treatments increased potassium. **Conclusion:** The three extracts produced distinct biochemical profiles rather than a uniform protective response. Date-seed extract showed the most favorable cardiac-biomarker pattern, whereas bean-seed extract was associated with pronounced hepatic-enzyme and electrolyte shifts. Orange-peel extract showed selective effects that differed between cardiac and hepatic endpoints.

*Corresponding author email: dalal.turki@qu.edu.iq

1. Introduction

Biochemical monitoring is central to the evaluation of drug-related organ responses. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) remain widely used indicators of hepatocellular and cholestatic responses, although their interpretation requires consideration of tissue distribution, enzyme turnover, and the biological context of exposure (1). Drug-related liver effects involve oxidative, mitochondrial, inflammatory, and membrane-associated processes, and conventional enzymes remain useful when they are interpreted alongside the exposure pattern and complementary biomarkers (2). In the cardiovascular system, cardiac troponins provide high specificity for myocardial injury, whereas CK-MB and myoglobin retain value for characterizing changes in myocardial protein release and the timing or magnitude of tissue stress (3).

Aspirin has a well-established pharmacological profile, but repeated exposure can influence gastric, hepatic, renal, redox, and inflammatory pathways in experimental animals. High-dose acetylsalicylic acid has been associated with increased transaminases, oxidative stress, and hepatorenal injury, whereas antioxidant co-treatment can modify the magnitude of these changes (4). In myocardial ischemia/reperfusion, aspirin can reduce myocardial enzyme release while simultaneously influencing inflammatory and gastric responses, illustrating that its biological effects are tissue- and context-dependent (5). Aspirin also affects mitochondrial bioenergetics and glutathione-dependent redox regulation under metabolic stress (6), and experimental work on hepatic regeneration has shown that acetylsalicylic acid can modify proliferative responses after liver injury (7). These observations support simultaneous evaluation of multiple biochemical domains rather than interpretation of a single marker in isolation.

Citrus peels are rich in flavanones, phenolic acids, and related antioxidants. Citrus sinensis peel preparations have shown hepatoprotective and antioxidant activity in experimental toxicology, with modulation of aminotransferases, oxidative stress, and inflammatory mediators (8). Orange-peel extract has also attenuated cyclophosphamide-associated injury in liver, kidney, and heart through antioxidant and immunoregulatory effects (9), while Citrus reticulata peel extract reduced abamectin-associated oxidative and hepatic injury in rats (10). Citrus-peel preparations have additionally been linked to improved hepatic lipid metabolism and reduced oxidative stress in high-fat-diet studies (11). Direct chemical studies confirm substantial radical-scavenging activity in orange-peel constituents (12), and recent work with Citrus sinensis extracts has demonstrated effects on metabolic dysregulation, inflammatory cytokines, and oxidative stress in female rats (13). Orange-peel phytochemistry commonly includes gallic acid, flavonoids, and other redox-active constituents (14). Hesperidin, one of the characteristic citrus flavonoids, has also reduced troponin I and CK-MB elevations in experimental cardiotoxicity (15).

Date seeds represent another concentrated source of phenolics, flavonoids, dietary fiber, and antioxidant constituents (16). In rats, date-seed extracts have reduced paracetamol-associated changes in ALT, AST, ALP, oxidative stress, and antioxidant defenses (17), and date-seed supplementation has improved antioxidant status in chemically induced metabolic injury (18). Extracts from Saudi date cultivars have reduced hepatic steatosis, inflammatory markers, and oxidative imbalance in high-fat-diet-fed rats (19). Cardiac studies further indicate that date-seed preparations can reduce CK-MB and related cardiac-toxicity markers under aflatoxin exposure (20), while recent work has shown parallel hepatic and cardiac benefits in a heptaminol-toxicity setting (21). The high content of free and bound polyphenols in date seeds provides a mechanistic basis for these observations (22), and phenolic profiles vary substantially among cultivars and ripening stages while retaining

antioxidant potential (23). Contemporary reviews therefore identify date-palm by-products as promising multifunctional food-derived sources of antioxidant and anti-inflammatory compounds (24).

Common-bean seeds also contain phenolic acids, flavonoids, anthocyanins, and other antioxidant constituents. Considerable cultivar-dependent variation in total phenolics and antioxidant capacity has been documented in *Phaseolus vulgaris* seeds (25). Phenolic-enriched extracts from black and pinto beans show both antioxidant and anti-inflammatory activity (26), and black-bean polyphenolic extracts exhibit strong free-radical-scavenging properties (27). Bean extracts can reduce lipid accumulation and lipid oxidation in hepatocyte systems (28), while polyphenol-enriched common-bean extracts reduce reactive oxygen species under chemical stress (29). Comparative metabolomic work also supports a major contribution of polyphenols and related metabolites to the antioxidant activity of common beans (30).

Against this background, the present study compared hot ethanolic extracts of orange peel, date seeds, and common-bean seeds under a common 30-day aspirin exposure. Cardiac biomarkers, hepatic enzymes, and serum minerals were assessed concurrently to determine whether the three plant preparations produced similar or distinct biochemical response profiles.

2. Materials and Methods

2.1. Plant materials and preparation of hot ethanolic extracts

Fresh orange peels and date seeds (if available) and dry common beans were cleaned, dried, and milled. Each was extracted with 70% ethanol at a ratio of 1:10 (w/v) and 60°C for 2 hours with constant mixing. Extraction was done in three batches and filtrates were combined. Ethanol was removed with a rotary vacuum evaporator at a temperature below 45°C. The residue was stored in an airtight container at 4°C and suspended in distilled water at a dose of 150mg/kg body weight.

2.2. Experimental animals and husbandry

A total of twenty five (25) adult albino rats with an approximate body weight of 250g were used for the experiment. The rats were kept under standard laboratory conditions for a period of 7 days prior to the start of the experiment. Standard lab food and water were made available to the rats for the period of the experiment. The rats were observed daily for the period of the experiment.

2.3. Experimental Groups and Treatment Schedule

The experimental rats were evenly distributed to five groups (n=5 per group). Group C (the untreated control) was administered the vehicle. Group A administered 20 mg/kg aspirin. Group B administered orange peel extract at 150 mg/kg and 20 mg/kg of aspirin. Group T was administered date-seed extract at 150 mg/kg and 20 mg/kg of aspirin. Group F was administered common bean-seed extract at 150 mg/kg and 20 mg/kg of aspirin. All administered treatments were conducted orally and for a period of 30 consecutive days. The suspensions of the plant extracts and aspirin were prepared on the day of administration.

2.4. Blood Collection and Serum Preparation

At the end of the 30th day, rats were allowed to fast, and water was given ad libitum. Blood was obtained from the rats under light anesthesia and allowed to clot. The serum was obtained after centrifugation (at 3000 x g for 10 minutes). The serum was immediately frozen (at -20°C) until analysis.

2.5. Cardiac biomarkers

Serum myoglobin, cardiac troponin I, and CK-MB mass concentrations were quantified by enzyme-linked immunoassay using standard curves prepared for each analyte. Samples and standards were processed in duplicate, and absorbance was read at the wavelength specified for the assay reaction. Concentrations were calculated from the calibration curves and expressed as ng/mL.

2.6. Hepatic enzyme activities

Serum ALT and AST activities were determined by kinetic aminotransferase procedures based on substrate-dependent transamination reactions, and ALP activity was determined by the p-nitrophenyl-phosphate method under alkaline conditions. Enzyme activities were expressed as U/L.

2.7. Serum minerals and electrolytes

Serum sodium, potassium, and chloride were determined by ion-selective electrode measurement. Total calcium was determined by a colorimetric complexation procedure. Sodium, potassium, and chloride were expressed as mmol/L and calcium as mg/dL.

2.8. Statistical analysis

Results are presented as mean $\pm$ standard deviation (SD), with five animals in each group. Group differences were evaluated by one-way analysis of variance followed by Fisher's least significant difference (LSD) comparison at $P < 0.05$. The supplied LSD thresholds were 0.331 for myoglobin, 0.014 for troponin I, 0.294 for CK-MB, 131.6 for ALT, 110.5 for AST, 24.02 for ALP, 1.29 for potassium, 2.93 for chloride, 4.48 for sodium, and 2.41 for calcium. Means carrying different superscript letters were interpreted as significantly different at $P < 0.05$.

2.9. Ethical statement

Animal handling and experimental procedures followed institutional animal-care requirements and internationally accepted principles for the humane care and use of laboratory animals. All procedures were performed to minimize discomfort and to use the minimum number of animals required for the biochemical comparisons.

3. Results

3.1. Cardiac biomarkers

Cardiac biomarkers showed clear treatment-specific differences (Table 1; Figure 1). Myoglobin was highest in the aspirin-only and orange-peel plus aspirin groups (1.10 ± 0.12 ng/mL for each; superscript a), whereas the control and date-seed plus aspirin groups showed lower values (0.668 ± 0.09 and 0.72 ± 0.09 ng/mL, respectively; superscript b). The bean-seed plus aspirin group was intermediate (0.82 ± 0.12 ng/mL; superscript ab). Troponin I was highest after orange-peel plus aspirin (0.026 ± 0.006 ng/mL; a), followed by bean-seed plus aspirin (0.024 ± 0.005 ng/mL; ab) and date-seed plus aspirin (0.016 ± 0.004 ng/mL; ab). The control value was 0.011 ± 0.002 ng/mL (bc), while aspirin alone was 0.020 ± 0.005 ng/mL (c). CK-MB was highest in the orange-peel plus aspirin group (0.90 ± 0.08 ng/mL; a). The lowest CK-MB values occurred in the control and date-seed groups (0.468 ± 0.06 and 0.46 ± 0.15 ng/mL; b), with aspirin alone and bean-seed plus aspirin occupying the intermediate significance class (ab).

Table 1. Serum cardiac biomarkers after 30 days of treatment.

Group	Myoglobin (ng/mL)	Troponin I (ng/mL)	CK-MB (ng/mL)
C: Control	0.668 ± 0.09b	0.011 ± 0.002bc	0.468 ± 0.06b
A: Aspirin	1.1 ± 0.12a	0.020 ± 0.005c	0.74 ± 0.1ab
B: Orange peel + aspirin	1.1 ± 0.12a	0.026 ± 0.006a	0.9 ± 0.08a
T: Date seed + aspirin	0.72 ± 0.09b	0.016 ± 0.004ab	0.46 ± 0.15b
F: Bean seed + aspirin	0.82 ± 0.12ab	0.024 ± 0.005ab	0.62 ± 0.07ab
LSD (P<0.05)	0.331	0.014	0.294

Values are mean ± SD (n=5). Within each column, means with different superscript letters differ significantly according to Fisher's LSD at P<0.05.

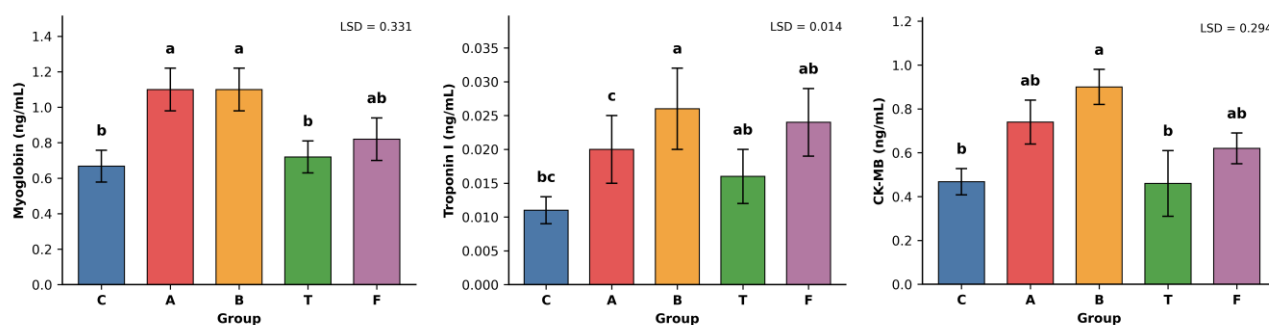


Figure 1. Serum cardiac biomarkers in the five experimental groups. Bars represent mean ± SD (n=5). Different letters above bars denote significant differences by Fisher's LSD at P<0.05. C, control; A, aspirin; B, orange-peel extract + aspirin; T, date-seed extract + aspirin; F, bean-seed extract + aspirin. Each group is shown with a distinct color consistently across all figures.

3.2. Hepatic enzyme activities

The hepatic enzyme pattern differed from the cardiac-biomarker profile (Table 2; Figure 2). ALT was highest in the bean-seed plus aspirin group (486.4±42.7 U/L; a), followed by date-seed plus aspirin (400.4±51.5 U/L; ab) and control (353.66±4.47 U/L; b). Aspirin alone and orange-peel plus aspirin had the lowest ALT activities (203.8±26.8 and 207.8±68.6 U/L; c). AST showed an analogous pattern, with bean-seed plus aspirin reaching 526.6±35.8 U/L (a), date-seed plus aspirin and control at 376.4±46.3 and 333.33±6.58 U/L (b), and aspirin alone and orange-peel plus aspirin at 164.4±6.65 and 208.0±59.1 U/L (c). ALP displayed a different ordering: aspirin alone and orange-peel plus aspirin were highest (165.8±6.14 and 149.6±11.5 U/L; a), the date-seed group was intermediate (144.4±12.09 U/L; ab), the bean-seed group was lower (124.2±1.80 U/L; b), and control showed the lowest activity (53.332±3.11 U/L; c).

Table 2. Serum hepatic enzyme activities after 30 days of treatment.

Group	ALT (U/L)	AST (U/L)	ALP (U/L)
C: Control	353.66 ± 4.47b	333.33 ± 6.58b	53.332 ± 3.11c
A: Aspirin	203.8 ± 26.8c	164.4 ± 6.65c	165.8 ± 6.14a
B: Orange peel + aspirin	207.8 ± 68.6c	208.0 ± 59.1c	149.6 ± 11.5a
T: Date seed + aspirin	400.4 ± 51.5ab	376.4 ± 46.3b	144.4 ± 12.09ab
F: Bean seed + aspirin	486.4 ± 42.7a	526.6 ± 35.8a	124.2 ± 1.8b
LSD (P<0.05)	131.6	110.5	24.02

Values are mean ± SD (n=5). Within each column, means with different superscript letters differ significantly according to Fisher's LSD at P<0.05.

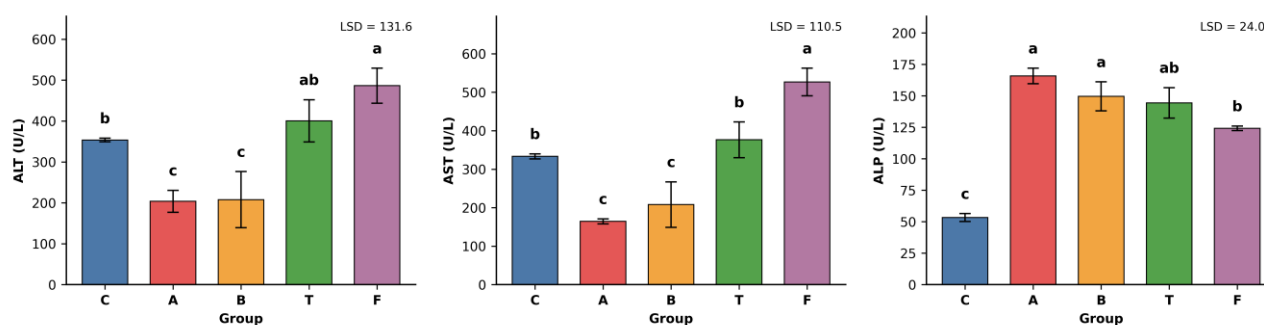


Figure 2. Serum ALT, AST, and ALP activities. Bars represent mean ± SD (n=5). Different letters above bars denote significant differences by Fisher's LSD at P<0.05. Group abbreviations and colors are identical to Figure 1.

3.3. Serum mineral and electrolyte concentrations

Serum mineral concentrations also exhibited distinct treatment-dependent patterns (Table 3; Figure 3). Potassium was highest in date-seed plus aspirin (7.58 ± 0.77 mmol/L), bean-seed plus aspirin (7.06 ± 0.55 mmol/L), and aspirin alone (6.60 ± 0.13 mmol/L), all in significance class a. Control and orange-peel plus aspirin were lower (5.068 ± 0.20 and 4.76 ± 0.05 mmol/L; b). Chloride reached its highest value in the bean-seed group (110.2 ± 0.37 mmol/L; a); aspirin and date-seed groups were intermediate (104.4 ± 0.67 and 104.6 ± 1.72 mmol/L; b), while control and orange-peel groups were lower (103.66 ± 0.96 and 103.6 ± 0.67 mmol/L; c). Sodium was markedly elevated only in the bean-seed group (155.6 ± 2.50 mmol/L; a); all other groups shared significance class b. Calcium was lowest in control (8.40 ± 0.45 mg/dL; b), highest in orange-peel plus aspirin and bean-seed plus aspirin (11.32 ± 0.65 and 11.02 ± 1.36 mg/dL; a), and intermediate in aspirin and date-seed groups (10.76 ± 0.32 and 10.18 ± 0.86 mg/dL; ab).

Table 3. Serum mineral and electrolyte concentrations after 30 days of treatment.

Group	K (mmol/L)	Cl (mmol/L)	Na (mmol/L)	Ca (mg/dL)
C: Control	5.068 ± 0.2b	103.66 ± 0.96c	145.0 ± 0.31b	8.4 ± 0.45b
A: Aspirin	6.6 ± 0.13a	104.4 ± 0.67b	145.8 ± 0.38b	10.76 ± 0.32ab
B: Orange peel + aspirin	4.76 ± 0.05b	103.6 ± 0.67c	142.2 ± 1.72b	11.32 ± 0.65a
T: Date seed + aspirin	7.58 ± 0.77a	104.6 ± 1.72b	143.0 ± 1.37b	10.18 ± 0.86ab
F: Bean seed + aspirin	7.06 ± 0.55a	110.2 ± 0.37a	155.6 ± 2.5a	11.02 ± 1.36a
LSD (P<0.05)	1.29	2.93	4.48	2.41

Values are mean ± SD (n=5). Within each column, means with different superscript letters differ significantly according to Fisher's LSD at P<0.05.

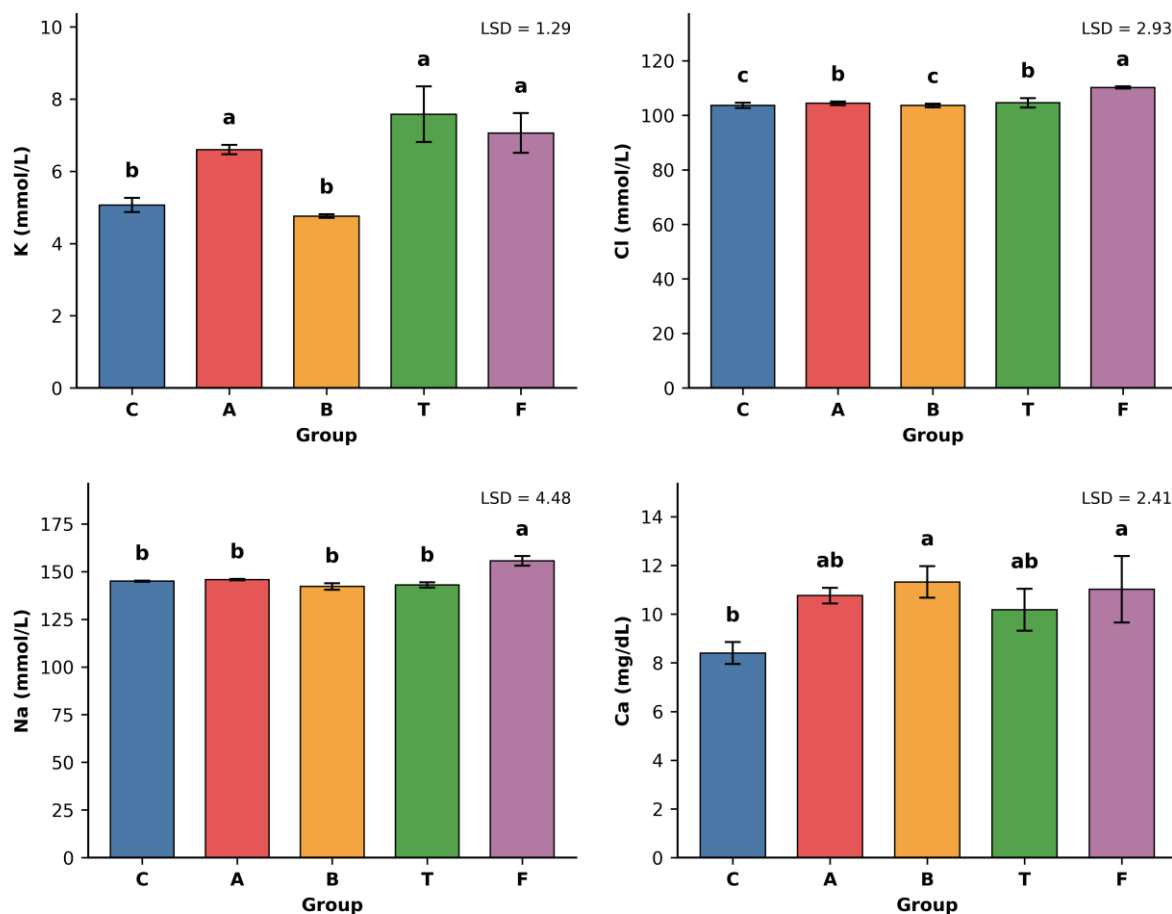


Figure 3. Serum potassium, chloride, sodium, and calcium concentrations. Bars represent mean ± SD (n=5). Different letters above bars denote significant differences by Fisher's LSD at P<0.05. Group abbreviations and colors are identical to Figure 1.

4. Discussion

The present findings show that the three plant extracts did not produce a single common pattern across the measured systems. Instead, cardiac biomarkers, hepatic enzymes, and serum minerals responded differently to each treatment. This distinction is important because serum enzyme activity reflects tissue leakage, synthesis, clearance, and metabolic state rather than a single universal index of tissue damage. ALT, AST, and ALP therefore require integrated interpretation (1,2), while troponin I, CK-MB, and myoglobin provide complementary information regarding myocardial protein release (3). The strongest cardiac pattern in the current study was associated with date-seed treatment, whereas the most pronounced aminotransferase and electrolyte shifts occurred with bean-seed treatment.

The aspirin-only group showed increased myoglobin and intermediate CK-MB relative to control, while troponin I shared a significance class with control. These findings indicate a modest cardiac biochemical response at 20 mg/kg over 30 days rather than the broad injury pattern reported after substantially higher aspirin exposures. Experimental aspirin toxicity is dose- and context-dependent: short high-dose administration can increase transaminases and oxidative injury (4), yet aspirin can also reduce myocardial enzyme release in ischemia/reperfusion settings (5) and can modify mitochondrial and glutathione-dependent metabolism (6). The lower ALT and AST values observed with aspirin alone in the present study therefore should not be interpreted as a stand-alone hepatoprotective signal. Aspirin is capable of altering hepatic cell responses and regenerative activity (7), and the concurrent elevation of ALP in the aspirin group demonstrates that individual hepatic markers can move in different directions under the same exposure.

Orange-peel extract produced a mixed profile. Its ALT and AST activities remained in the same low significance class as aspirin alone, but ALP remained high, and the cardiac markers did not improve: myoglobin remained at 1.10 ± 0.12 ng/mL, troponin I was the highest of all groups, and CK-MB also reached the highest value. This contrasts with many studies reporting antioxidant and hepatoprotective actions of *Citrus sinensis* peel (8,9), *Citrus reticulata* peel (10), and citrus-peel preparations in metabolic liver injury (11). Orange peel contains multiple radical-scavenging compounds (12), and *Citrus sinensis* extracts have demonstrated anti-inflammatory and antioxidant effects in female rats (13). Its phytochemical makeup varies and can consist of gallic acid, flavonoids and other phenolics (14). Hesperidin provides cardioprotection (15) and other flavonoids likely provide similar effects; however, there exist other constituents of the peel that may provide cardioprotection and/or hepatoprotection as do other constituents of orange peel. Therefore, effects of orange peel on cardioprotection may vary and depends on the specific effect being considered.

Extracts of date seeds provided the best cardioprotection. Myoglobin and CK-MB levels were considered low and insignificant compared to controls. Serum levels of Troponin I were less than other participants. The date seeds are rich in phytochemicals and provide potent antioxidant and anti-inflammatory activity (16). Improvements in the redox status have been reported with date seeds (18). Date seeds have been shown to ameliorate hepatic steatosis and inflammation in animal studies (19). Date seed extracts have reduced cardiotoxicity in combination with aflatoxin (20). Other studies have shown date seed extracts provide hepatocardioprotection in combination with other hepatotoxic agents (21). The varied activity of date seed extracts is attributed to differences in raw materials, extraction and processing methods (22,23).

Bean seeds provided intermediate cardioprotection with the largest changes observed with liver function. ALT, AST, sodium and chloride levels were considerably increased. Potassium and calcium levels were notably reduced. Common beans have high concentrations of phenolic compounds and exhibit potent

antioxidant activity. Extracts of black and pinto beans have antioxidant and anti-inflammatory activities. Extracts of beans can reduce lipid accumulation. Other extracts of plant origin have the ability to block reactive oxygen species. Extracts of plant and bean origins have diverse bioactive metabolites. Bean extracts exhibit potent antioxidant activity. In the current study, various enzymes in the liver were most likely, altered due to the antioxidant potential of the bean extracts. Treatment-related changes in levels of liver enzymes along with disruption of the electrolyte balance in the blood, likely occurred due to the metabolic effects of the bean extracts, which were examined in conjunction with Aspirin. The effect of bean extracts is likely to be greater in combination with Aspirin.

The bean-seed group, along with date-seed group, reduced AST and ALT. The combination of orange peel and Aspirin showed the greatest alterations in electrolyte levels. The highest levels of calcium were observed with the combination of orange peel and Aspirin. The treatment groups altered the levels of the electrolytes in blood probably due to the plant extracts or due to the metabolites formed as a result of interactions between plant extracts and Aspirin. The observed changes in serum electrolyte levels may be due to altered gastrointestinal absorption and/or renal function. The combination of bean extracts and Aspirin likely altered the activity of serum liver enzymes.

Considering the effects of ionic balance on cardiac excitability and hepatic metabolism, variations in blood electrolytes should be of primary importance in interpreting an case record forms. As such, the author suggests that the analysis of an case record forms should extend beyond a simple observation.(1)

Based on data presented in the case record forms, author suggested that the most favorable serum cardiac-biomarker pattern is associated with treatment containing date-seed extract, and that the cardiac effects of extracts were not improved by the co-administration of aspirin. Orange-peel extract and bean-seed extract altered the cardiac biomarkers and liver function test respectively, and both extracts have selective organ effects. The results of this study indicate that food extracts contain numerous active ingredients, and depending upon the co-administered ingredient, may have effects on multiple organ systems.

6. Conclusion

Hot ethanolic extracts of orange peel, date seeds, and common-bean seeds produced clearly different biochemical responses during 30 days of aspirin exposure in female rats. Date-seed extract showed the most favorable cardiac profile, with low myoglobin and CK-MB values close to control. Orange-peel extract maintained low ALT and AST activities but did not improve the measured cardiac biomarkers and retained high ALP activity. Bean-seed extract produced the highest ALT and AST activities and the most prominent sodium and chloride elevations. These findings demonstrate that the biological effects of the three plant preparations are organ- and endpoint-specific and that date-seed extract warrants particular attention when the objective is preservation of cardiac biochemical status during aspirin exposure.

Declarations

Conflict of interest: None declared.

Funding: No external funding.

Data availability: All numerical data supporting the findings are presented in the tables and figures of this article.

Author contribution: Dalal Turki Shattnan Al Gabri contributed to the experimental work, data acquisition, analysis, interpretation, and preparation of the manuscript. Mohammed M. Yaseen Investigation; Methodology; Formal analysis; Validation; Visualization; and Writing – review and editing

References

1. Thakur S, Kumar V, Das R, Sharma V, Mehta DK. Biomarkers of hepatic toxicity: an overview. *Curr Ther Res Clin Exp*. 2024;100:100737.
2. Fu S, Wu D, Jiang W, Li J, Long J, Jia C, Zhou T. Molecular biomarkers in drug-induced liver injury: challenges and future perspectives. *Front Pharmacol*. 2020;10:1667.
3. Ragusa R, Masotti S, Musetti V, Rocchiccioli S, Prontera C, Perrone M, Passino C, Clerico A, Caselli C. Cardiac troponins: mechanisms of release and role in healthy and diseased subjects. *Biofactors*. 2023;49(2):351-364.
4. El-Sheikh SMA, Bahaa HM, Galal AAA, Metwally MMM, Said MA, Alattar RH, Fahmy EM. Gastroprotective, hepatoprotective, and nephroprotective effects of thymol against the adverse effects of acetylsalicylic acid in rats: biochemical and histopathological studies. *Saudi J Biol Sci*. 2022;29(6):103289.
5. Dong Z, Yang L, Jiao J, Jiang Y, Li H, Yin G, Yang P, Sun L. Aspirin in combination with gastrodin protects cardiac function and mitigates gastric mucosal injury in response to myocardial ischemia/reperfusion. *Front Pharmacol*. 2022;13:995102.
6. John A, Amiri L, Shafarin J, Tariq S, Adeghate E, Howarth FC, Raza H. Alterations in energy metabolism, mitochondrial function and redox homeostasis in GK diabetic rat tissues treated with aspirin. *Life (Basel)*. 2022;12(1):104.
7. Biondo-Simões MLP, Pessini VCA, Ichi CA, Robes RR, Ioshii S. Acetylsalicylic acid (Aspirin) and liver regeneration: experimental study in rats. *Rev Col Bras Cir*. 2021;48:e20213164.
8. Abou Baker DH, Ibrahim BMM, Abdel-Latif Y, Hassan NS, Hassan EM, El Gengaihi S. Biochemical and pharmacological prospects of *Citrus sinensis* peel. *Heliyon*. 2022;8(8):e09979.
9. Abdelghffar EA, El-Nashar HAS, Al-Mohammadi AGA, Eldahshan OA. Orange fruit (*Citrus sinensis*) peel extract attenuates chemotherapy-induced toxicity in male rats. *Food Funct*. 2021;12(19):9443-9455.
10. Rahib A, Karhib MM, Nasr HM, El-Sayed RA, Abdel-Daim MM, Jebur AB, El-Demerdash FM. Citrus reticulata peel extract mitigates oxidative stress and liver injury induced by abamectin in rats. *Tissue Cell*. 2024;87:102321.
11. Lee GH, Peng C, Park SA, Hoang TH, Lee HY, Kim J, Kang SI, Lee CH, Lee JS, Chae HJ. Citrus peel extract ameliorates high-fat diet-induced NAFLD via activation of AMPK signaling. *Nutrients*. 2020;12(3):673.
12. Ajeena SJ, Al-Zaidi RMK, Hadi MT, Ghazal MM. Study of the antioxidant activity of some active compounds in orange peels. *Cell Mol Biol (Noisy-le-grand)*. 2024;70(10):161-166.
13. Schmitt EG, Schreiner GE, Dos Santos LS, de Oliveira CP, Pereira CB, Sarmiento SMM, Klock C, Petry CC, Denardin ELG, Gonçalves IL, Malheiros RT, Manfredini V. Moro orange (*Citrus sinensis* (L.) Osbeck)

extract mitigates metabolic dysregulation, inflammation, oxidative stress, and adipose tissue hyperplasia in obese rats. *Int J Mol Sci.* 2025;26(12):5727.

14. Abd El-Aziz NM, Shehata MG, Alsulami T, Badr AN, Elbakatoshy MR, Ali HS, El-Sohaimy SA. Characterization of orange peel extract and its potential protective effect against aluminum chloride-induced Alzheimer's disease. *Pharmaceuticals (Basel).* 2023;16(1):12.

15. Alharbi FK, Alshehri ZS, Alshehri FF, Alhajlah S, Khalifa HA, Dahran N, Ghonimi WAM. The role of hesperidin as a cardioprotective strategy against doxorubicin-induced cardiotoxicity: the antioxidant, anti-inflammatory, antiapoptotic, and cytoprotective potentials. *Open Vet J.* 2023;13(12):1718-1728.

16. Alkhoori MA, Kong ASY, Aljaafari MN, Abushelaibi A, Lim SHE, Cheng WH, Chong CM, Lai KS. Biochemical composition and biological activities of date palm (*Phoenix dactylifera* L.) seeds: a review. *Biomolecules.* 2022;12(11):1626.

17. Bouhlali EDT, Derouich M, Hmidani A, Bourkhis B, Khouya T, Filali-Zegzouti Y, Alem C. Protective effect of *Phoenix dactylifera* L. seeds against paracetamol-induced hepatotoxicity in rats: a comparison with vitamin C. *ScientificWorldJournal.* 2021;2021:6618273.

18. Abbassi R, Pontes MC, Dhibi S, Duarte Filho LAMS, Othmani S, Bouzenna H, Almeida JRGS, Hfaiedh N. Antioxidant properties of date seeds extract (*Phoenix dactylifera* L.) in alloxan induced damage in rats. *Braz J Biol.* 2023;83:e274405.

19. Zarie AA, Osman MA, Alshammari GM, Hassan AB, Yagoub AEA, Yahya MA. Saudi date cultivars' seed extracts inhibit developing hepatic steatosis in rats fed a high-fat diet. *Saudi J Biol Sci.* 2023;30(9):103732.

20. Khalil HMA, Eid WAM, El-Nablaway M, El Nashar EM, Al-Tarish JS, El Henafy HMA. Date seeds powder alleviate the aflatoxin B1 provoked heart toxicity in male offspring rat. *Sci Rep.* 2024;14(1):30480.

21. Abbassi R, Bouzenna H, Badraoui R, Atwan M, Brahmi F, Feriani A, Siddiqui AJ, Adnan M, Mohajja A, Choura S, Chamkha M, Hfaiedh N. Heptaminol-induced metabolic liver and cardiac injuries in rats: phytochemical screening, experimental, computational modelling and pharmacological study of *Phoenix dactylifera* seeds. *Arch Physiol Biochem.* 2025;131(5):859-873.

22. Bettaieb I, Benabderrahim MA, Rodríguez Arcos R, Jiménez Araujo AJ, Elfalleh W. Date seeds (*Phoenix dactylifera*): antioxidant potential and profile of free and bound polyphenols from different cultivars. *Chem Biodivers.* 2023;20(6):e202300179.

23. Shi L, Liu Z, Gonzalez Viejo C, Ahmadi F, Dunshea FR, Suleria HAR. Comparison of phenolic composition in Australian-grown date fruit (*Phoenix dactylifera* L.) seeds from different varieties and ripening stages. *Food Res Int.* 2024;181:114096.

24. Alu'datt MH, Rababah T, Tranchant CC, Al-U'datt D, Gammoh S, Alrosan M, Bani-Melhem K, Aldughpassi A, Alkandari D, AbuJalban D. Date palm (*Phoenix dactylifera*) bioactive constituents and their applications as natural multifunctional ingredients in health-promoting foods and nutraceuticals: a comprehensive review. *Compr Rev Food Sci Food Saf.* 2025;24(1):e70084.

25. Rodríguez Madrera R, Campa Negrillo A, Suárez Valles B, Ferreira Fernández JJ. Phenolic content and antioxidant activity in seeds of common bean (*Phaseolus vulgaris* L.). *Foods.* 2021;10(4):864.

26. Fonseca Hernández D, Mojica L, Berhow MA, Brownstein K, Lugo Cervantes E, Gonzalez de Mejia E. Black and pinto beans (*Phaseolus vulgaris* L.) unique Mexican varieties exhibit antioxidant and anti-inflammatory potential. *Food Res Int.* 2023;169:112816.
27. Fonseca-Hernández D, Lugo-Cervantes EC, Escobedo-Reyes A, Mojica L. Black bean (*Phaseolus vulgaris* L.) polyphenolic extract exerts antioxidant and antiaging potential. *Molecules.* 2021;26(21):6716.
28. Dibwe DF, Kitayama E, Oba S, Takeishi N, Chiba H, Hui SP. Inhibition of lipid accumulation and oxidation in hepatocytes by bioactive bean extracts. *Antioxidants (Basel).* 2024;13(5):513.
29. Fonseca Hernandez D, Mojica L, Lugo Cervantes E, Gonzalez de Mejia E. Common bean polyphenolic enriched extracts decrease reactive oxygen species induced by heavy metals and polycyclic aromatic hydrocarbons in Hs27 and Hs68 human fibroblasts. *Food Chem.* 2024;459:140371.
30. Zhang W, Zhao Y, Yang H, Liu Y, Zhang Y, Zhang Z, Li Y, Wang X, Xu Z, Deng J. Comparison analysis of bioactive metabolites in soybean, pea, mung bean, and common beans: reveal the potential variations of their antioxidant property. *Food Chem.* 2024;457:140137.