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INVESTIGATING THE THERAPEUTIC POTENTIAL OF *Ficus carica* LEAVES EXTRACT IN A RAT MODEL OF INDUCED MYOCARDIAL INFARCTION

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ABSTRACT

Myocardial infarction damages the myocardium due to oxidative stress from increased reactive oxygen species during ischemia, leading to reduced antioxidant defenses and lipid peroxidation. Due to limitations of conventional protective drugs like angiotensin-converting enzyme inhibitors and beta-blockers, phytomedicines are receiving more attention. The purpose of our study was to investigate the therapeutic potential of *Ficus carica* (FC) leaves extract against a high-fat diet coupled with isoproterenol-induced myocardial infarction in the rat model. The ethanolic extract of FC leaves was prepared to evaluate the phytochemical constituents and therapeutic effects. The experimental trial consists of 32 Albino Wistar rats, which were randomly allocated into four groups (n = 8 per group) in a completely randomized design (CRD). Group one served as the negative control (NC) group, receiving a normal diet, while the second group was the positive control (PC) group, receiving isoproterenol subcutaneously. Group three served as the standard (STD) group and received metoprolol orally. The fourth group was the *Ficus carica* leaves extract (FCLE) treatment group, administered FCLE orally. The serum samples were collected to perform biochemical analyses at the end of the experiment. Hematoxylin and eosin staining of the heart and aorta tissue was performed. All obtained data were subjected to statistical analysis. FCLE treatment group significantly ($p \leq 0.05$) improved cardiac biomarkers, restored oxidative balance, and normalized hepatic, renal, and systemic biochemical markers compared to the positive control group. Our findings highlight FCLE's potential as a therapeutic agent for myocardial infarction and support further investigation into its clinical applications.

Keywords: Heart attack, natriuretic peptide, aminotransferase, flavonoids, antioxidants

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INTRODUCTION

The heart, being an indispensable organ for survival, serves as the central pump of blood circulation and continuously beats to ensure the supply of energy and exchange of nutrients in our body (Sun *et al.*, 2021). If the heart doesn't function properly, various cardiovascular diseases (CVDs), including conditions like hypertension, atherosclerosis, and ischemic heart disease (IHD), leading to heart attacks and strokes, may occur (Zhang *et al.*, 2022). Myocardial infarction (MI) is a serious cardiovascular condition leading to damage in the left ventricle due to prolonged ischemia (Feng et al., 2023). Myocardial infarction involves myocardial damage due to oxidative stress from increased reactive oxygen species during ischemia, leading to reduced antioxidant defenses and lipid peroxidation (Fan, 2019). According to the World Health Organization's prediction, annual deaths will rise globally from 18.1 million in 2010 to a staggering 24.2 million in 2030 due to CVDs (Kura *et al.*, 2020).

Myocardial infarction (MI) involves a complex pathophysiological process primarily driven by ischemia-induced oxidative stress (Yao *et al*., 2023). During MI, the obstruction of coronary blood flow leads to a critical reduction in oxygen supply to the myocardium, causing mitochondrial dysfunction and overproduction of reactive oxygen species (ROS) (Wal *et al*., 2023). These ROS include superoxide anions (O_2^-), hydroxyl radicals (OH), hydrogen peroxide (H_2O_2), and other reactive species that overwhelm the heart's endogenous antioxidant defenses (Li *et al*., 2022). Major sources of ROS during MI include the mitochondrial electron transport chain, NADPH oxidases, and enzymatic reactions involving xanthine oxidase and inflammatory cells (Xiang *et al*., 2021). Excessive ROS production leads to oxidative damage to cellular lipids, proteins, and DNA, thereby disrupting mitochondrial integrity and impairing ATP generation (Pietrangelo *et al*., 2025). This oxidative injury triggers mitochondrial permeability transition pore opening, calcium overload, and the activation of

apoptotic pathways, culminating in cardiomyocyte death (Das *et al*., 2025).

Isoproterenol, a synthetic nonselective β-adrenergic receptor agonist, acts upon the β1 adrenergic receptors in the heart (Abdelzaher *et al.*, 2021). The high doses of Isoproterenol can lead to oxidative stress in the myocardium, calcium overload, and energy depletion that causes MI (Yang *et al.*, 2022). Most used drugs for the management of MI, like angiotensin-converting enzyme (ACE) inhibitors and beta-adrenergic blocking agents, offer benefits, but their limitations fuel the search for alternative treatments (Shaito *et al.*, 2020).

Natural products have played an essential role in the development of therapies for CVDs, highlighting their potential in this realm. FC harbors a diverse phytochemical repertoire with ~125 identified compounds categorized into flavonoids, triterpenoids, volatiles, coumarins, and other classes that exhibit a broad spectrum of bioactivities, including anticholinesterase, anti-diabetic, and anticancer properties (Li *et al.*, 2021; Alsufyani *et al.*, 2023). Notably, fig leaves are rich in phenolic compounds, making them a natural source of antioxidants (Agatonovic *et al.*, 2023). The purpose of our study was to investigate the therapeutic potential of *Ficus carica* leaves extract (FCLE) against a high-fat diet coupled with isoproterenol-induced myocardial infarction in the rat model.

MATERIALS AND METHODS

Drugs and chemicals: Isoproterenol hydrochloride (Sigma-Aldrich, Catalog Number: I5627) was used to induce myocardial infarction. A high-fat diet (HFD) was prepared using hydrogenated vegetable ghee (Dalda Banaspati ghee, manufactured by Dalda Foods Pvt. Ltd., Pakistan) as the primary fat source. Metoprolol tartrate (Merol, manufactured by Atco Laboratories (Pvt.) Ltd., Karachi, Pakistan), was used as the standard treatment.

Leaves collection and extract preparation: Fresh leaves of *Ficus carica* (FC) were collected from healthy, mature trees growing in the University of Agriculture Faisalabad (UAF), Punjab, Pakistan, during September 2023. The leaves were identified by Professor Dr. Farooq Ahmad, Chairman, Department of Botany, UAF, and a voucher specimen (Table 3.1) was deposited at The Herbarium of the Department of Botany, UAF, and stored in the herbarium for future reference. Approximately 1.5 kg of FC leaves were shade-dried and ground to obtain a fine powder, followed by mixing 100 grams of *Ficus carica* leaves powder with 1 L of 70% ethanol at room temperature. The mixture was filtered through Whatman No. 1 filter paper, and the extract was concentrated using a rotary evaporator. The obtained extract was used for phytochemical analysis and trial purposes.

Table 1. Details of the medicinal plant

Botanical Name	English/Urdu Name	Family	Part Used	Herbarium Number
Ficus carica	Fig/ Injeer	Moraceae	Leaves	1017-3-23

Qualitative phytochemical analysis of FCLE: The presence of flavonoids and phenolic compounds was assessed using the ferric chloride test. Alkaloids were assessed by Mayer's test, while the presence of saponins was determined through the Foam test. Carbohydrates were identified using Molisch's test, and proteins were assessed with the Biuret test. Cardiac glycosides were tested using the Keller-Killani method. Quinones were detected by adding 1 mL of concentrated H_2SO_4 to 1 mL of extract, producing a red color, while phylobatannins were identified by treating 2 mL of hydroalcoholic extract with 2 mL of 1% HCl and heating, resulting in red precipitates (Harborne, 1984).

Ethical approval: The experiment was commenced after obtaining ethical approval (Approval number: 1547/ORIC, Date: 15/04/2024) from the Institutional Biosafety and Bioethics Committee (IBC) of the University of Agriculture Faisalabad, Pakistan, by following the guidelines outlined in the National Biosafety Rules 2005, Punjab Biosafety Rules 2014, Punjab Animal Health Act 2019, and the Bioethics protocol.

Experimental design: A total of 32 male Albino Wistar rats, weighing 200±20 grams, were obtained and maintained under standard laboratory conditions in the animal house of the Institute of Physiology and Pharmacology, UAF. Following a seven-day acclimatization period at 26°C±2°C and 40-60% humidity, the rats were randomly allocated into four groups (n=8 per group) using a completely randomized design (CRD). The experimental groups were the same as those described in (Khan *et al.,* 2025). Briefly, group one served as the negative control (NC) group, given a normal diet with water *ad libitum*. The other three groups received a high-fat diet for 14 days. After 14th day, the high-fat diet was replaced with a normal diet. The second group, named the positive control (PC) group, was induced with myocardial infarction by injecting 30 mg/kg/day of isoproterenol subcutaneously on days 13 and 14. The third group was the standard (STD) group, receiving metoprolol at 20 mg/kg/day orally from day 14

to 21, along with isoproterenol administration as in the second group. The fourth group, named the *Ficus carica* leaves extract (FCLE) group, was orally administered with FCLE at a dose of 300 mg/kg/day from day 14 to 21, concurrently with isoproterenol administration. The high-fat diet (HFD) was prepared by mixing 350 g of ghee with 650 g of basic chow diet per kilogram of feed. The chow diet was composed of maize (620 g), soybean meal (180 g), full-fat soybean (130.5 g), wheat offal (40 g), bone meal (20.5 g), lysine (2 g), methionine (3 g), and salt (4 g) per Kg. According to the manufacturer's specifications, Dalda ghee contains saturated fat (45 g), monounsaturated fat (40.5 g), polyunsaturated fat (14.5 g), and trans-fat (0.5 g) per 100 g.

Upon completion of the 21-day trial, five rats were decapitated via cervical dislocation in accordance with ethical procedures. Subsequently, the blood samples were collected and centrifuged at 4000 rpm to separate the serum for biochemical analyses. The aorta and heart tissues were carefully excised and preserved in 10% neutral buffered formalin for histopathological evaluation. Due to limited financial resources, only three samples per group were processed for analysis.

Body weight: Throughout the experiment, the body weight of each rat was recorded on days 0, 7, 14, and 21 through a digital weighing balance.

Oxidative stress and antioxidant markers: Serum total oxidative stress (TOS) was measured using the calorimetric method with the Elabscience® TOS assay kit; serum total antioxidant capacity (TAC) was measured using the calorimetric method with the Elabscience® TAS assay kit

Cardiac dysfunction markers: The levels of serum atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) were quantified by using the Abcam diagnostic ELISA kits.

Heart and liver function markers: Serum aspartate transaminase (AST) concentration was measured using a calorimetric method with the Bioclin® Transaminase AST diagnostic kit; serum alanine transaminase (ALT) concentration was measured using a calorimetric method with the Bioclin® Transaminase ALT diagnostic kit; and serum alkaline phosphatase (ALP) concentration was measured using calorimetric method with the Bioclin® Transaminase ALP kinetic diagnostic kit.

Serum bilirubin and total protein levels: Jendrassik-Grof was implicated in determining total bilirubin concentration using a commercially available kit of QCA®, Spain. Bioclin® Monoreagent Kit was used for total protein levels in serum.

Renal function markers: Urease-GLDH UV test was followed for the measurement of serum concentration of urea using Bioclinc® UV Kinetic Kit. The Bioclin® Kinetic kit was used to quantify the creatinine in serum by using a spectrophotometer. For the determination of uric acid (UA) concentration in serum, enzymatic colorimetry was followed by using the Bioclin® Monoreagent kit.

Histopathological Analysis: Histopathological analysis of heart and aorta tissues was performed using standard tissue processing and paraffin embedding techniques. Using a semi-automated rotary microtome (149MULTI0C1, Leica Biosystems Nussloch GmbH), 5 µm-thick sections of paraffin-embedded heart and aorta samples were prepared, mounted on slides, and stained with H&E. DPX was utilized as a mounting medium for glass coverslip placement on the stained tissue sections. Morphological studies were conducted by examining the slides under a light microscope at 10X, and images of the slides were captured using a camera through ToupView software (Hatipoglu *et al*., 2024).

Statistical analysis: All data are presented as mean ± standard error of the mean (SEM). Statistical analysis of the obtained data was performed using GraphPad Prism. Body weight measurements taken at multiple time points were analyzed using two-way analysis of variance (ANOVA) with repeated measures to evaluate the effects of time and treatment, followed by Tukey's post hoc test for multiple comparisons. The results of serum biochemical analysis were analyzed using one-way ANOVA followed by Tukey's post hoc test. The results were considered significantly different at the threshold of $p \leq 0.05$.

RESULTS

Qualitative phytochemical analysis of FCLE: The qualitative phytochemical analysis of the FCLE revealed the presence of bioactive compounds, including phenols, flavonoids, phylobatannins, terpenoids, gums and mucilages, tannins, and volatile oils, each contributing unique therapeutic properties, as shown in Table 2. Phenols and flavonoids are known for their antioxidant and protective roles against cellular damage. The presence of these compounds supports the potential of FCLE to exert antioxidant and cardioprotective effects. Cardiac glycosides, quinones, saponins, and alkaloids were absent in FCLE.

Body Weight: The body weight of rats was continuously monitored throughout the experimental period. A progressive increase in body weight was observed in rats fed a high-fat diet compared to those receiving a normal diet. The PC group significantly ($p \leq 0.05$) decreased body weight after day 14 to 21 due to isoproterenol-induced stress compared to the NC group. The STD and FCLE groups showed significant ($p \leq 0.05$) mitigation in weight

loss, indicating protective effects compared to the PC group, as illustrated in Figure 1.

Table 2. Qualitative phytochemical analysis of FCLE representing the presence or absence of phytochemical constituents

Plant Extract	Phytochemical Analysis (+ / -)		
Ficus carica leaves	-	Phenols	+
	-	Phylobatannins	+
	-	Quinones	-
	-	Terpenoids	+
	-	Flavonoids	+
	-	Cardiac Glycosides	-
	-	Gums and Mucilages	+
	-	Saponins	-
	-	Tannins	+
	-	Volatile Oils	+
	-	Alkaloids	-

(+) = Present, (-) = Absent

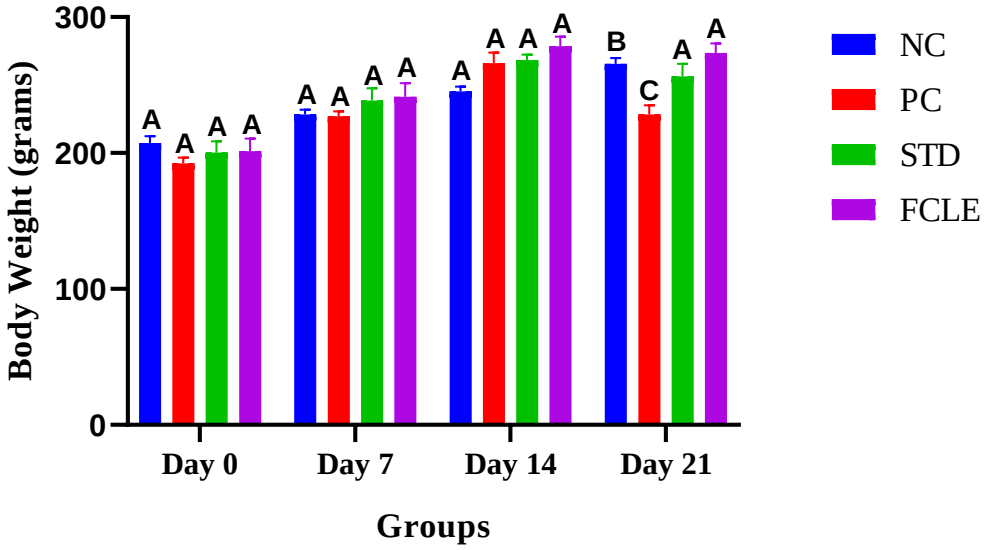

Figure 1. Changes in body weight in grams of rats measured on days 0, 7, 14, and 21 across different experimental groups. The means bearing different superscripts (A, B, C, D) exhibit statistically significant differences at the threshold of p≤0.05.

Oxidative Stress and Antioxidant Markers: Serum total oxidative stress (TOS) levels were measured to assess oxidative stress. The PC group demonstrates significantly (p≤0.05) elevated TOS levels in comparison with the NC group. The STD treatment group had significantly (p≤0.05) lower TOS levels in comparison with the PC group. The FCLE treatment group showed significantly (p≤0.05) reduced TOS levels due to its antioxidant effects, as illustrated in Figure 2(a).

Serum total antioxidant capacity (TAC) levels were measured to assess antioxidant capacity. The PC group exhibited a statistically significant (p≤0.05) decrease in TAC levels in comparison with the NC group. The STD treatment group had significantly (p≤0.05) increased TAC levels in comparison with the PC group. Similarly, the FCLE treatment group showed significantly (p≤0.05) elevated TAC levels as FCLE counteracts oxidative stress and improves overall antioxidant capacity, as illustrated in Figure 2(b).

Cardiac Dysfunction Markers: The PC group exhibited a statistically significant (p≤0.05) elevation in serum atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) levels in comparison with the NC group due to cardiac membrane stress. The STD group showed significantly (p≤0.05) decreased ANP and BNP levels in comparison with the PC group. The FCLE treatment group also showed significantly (p≤0.05) reduced levels of ANP and BNP, reducing the membrane stress due to its antioxidant potential, as illustrated in Figure 3.

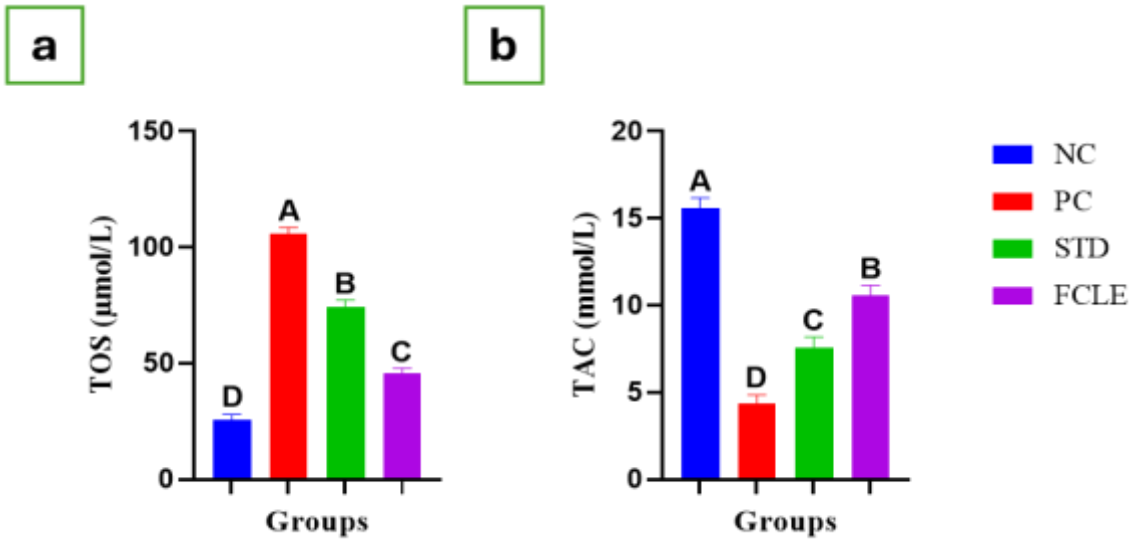

Figure 2 (a). Serum total oxidative stress (TOS) level in µmol/L (b). Serum total antioxidant capacity (TAC) level in mmol/L across different experimental groups. The means bearing different superscripts (A, B, C, D) exhibit statistically significant differences at the threshold of p≤0.05.

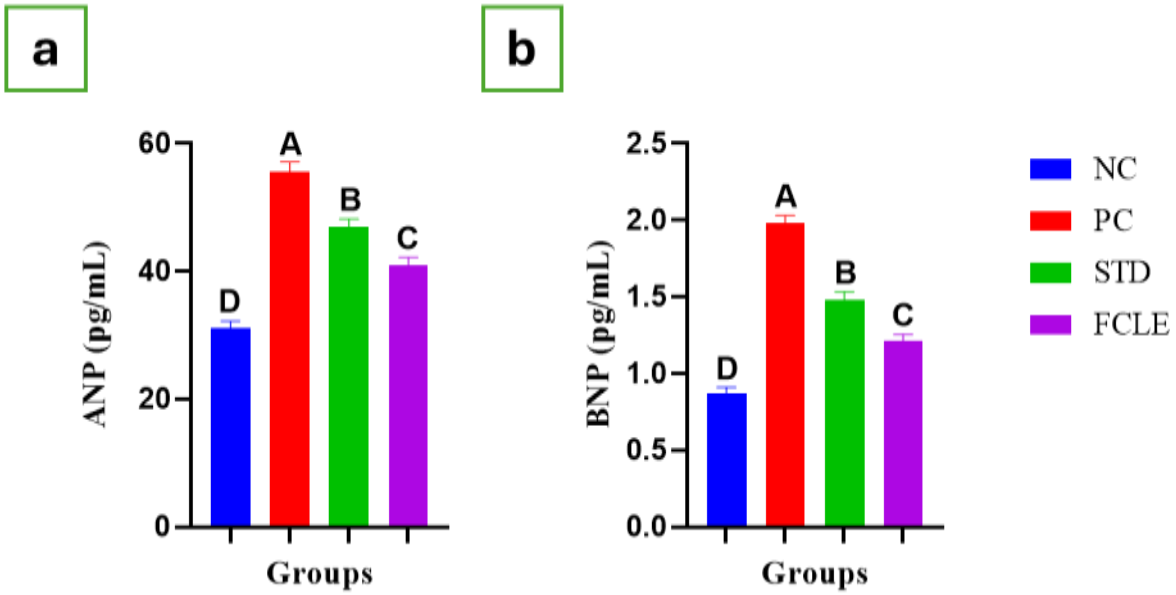

Figure 3 (a). Serum atrial natriuretic peptide (ANP) level in pg/mL (b). Serum brain natriuretic peptide (BNP) level in pg/mL across different experimental groups. The means bearing different superscripts (A, B, C, D) exhibit statistically significant differences at the threshold of p≤0.05.

Heart and Liver Function Markers: The PC group exhibited a statistically significant (p≤0.05) elevation in serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) levels in comparison with the NC group. The STD group showed a significant (p≤0.05) decrease in levels of AST, ALT, and ALP in comparison with the PC group. The FCLE treatment group also showed significantly (p≤0.05) reduced levels of AST, ALT, and ALP compared to the PC group, as illustrated in Figure 4.

Serum Total Bilirubin and Total Protein Levels: The PC group exhibited a statistically significant (p≤0.05) elevation in serum bilirubin level compared to the NC group. The STD group showed a significant (p≤0.05) decrease in bilirubin level in comparison with the PC group. The FCLE treatment group also showed

significantly ($p \leq 0.05$) reduced levels of bilirubin in comparison with the PC group, as illustrated in Figure 5(a). Serum total protein level was significantly ($p \leq 0.05$) reduced in the PC group in comparison with the NC group. The STD group showed a significant ($p \leq 0.05$) increase in total protein level in comparison with the PC group. The FCLE treatment group showed significantly ($p \leq 0.05$) elevated levels of total protein compared to the PC group, as illustrated in Figure 5(b).

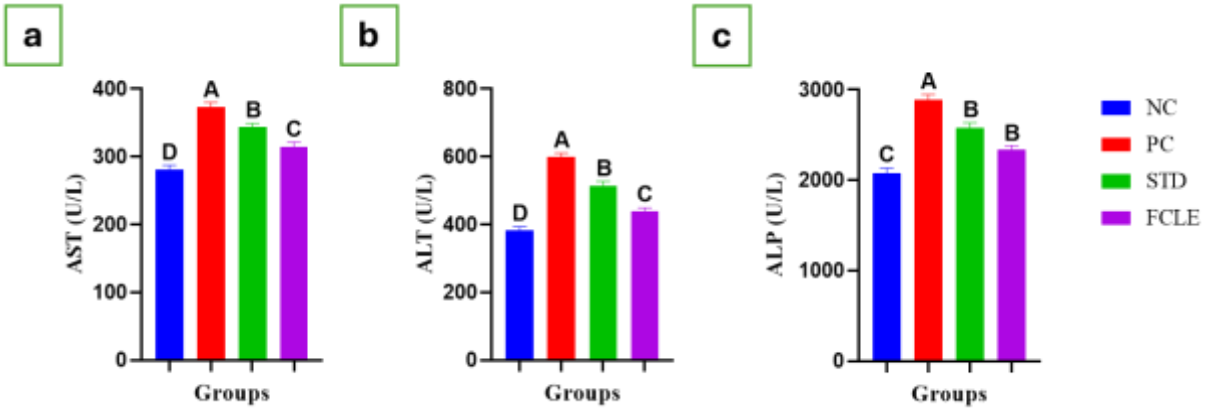

Figure 4 (a). Serum aspartate aminotransferase (AST) level in U/L (b). Serum alanine aminotransferase (ALT) level in U/L (c). Serum alkaline phosphatase (ALP) level in U/L across different experimental groups. The means bearing different superscripts (A, B, C, D) exhibit statistically significant differences at the threshold of $p \leq 0.05$.

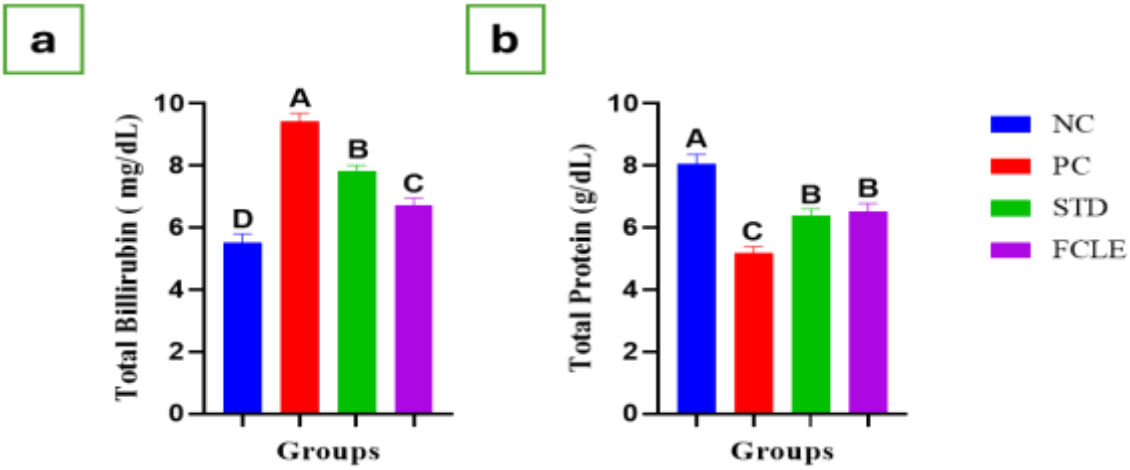

Figure 5 (a). Serum total bilirubin level in mg/dL (b). Serum total protein level in g/dL across different experimental groups. The means bearing different superscripts (A, B, C, D) exhibit statistically significant differences at the threshold of $p \leq 0.05$.

Renal Function Markers: The PC group exhibited a statistically significant ($p \leq 0.05$) elevation in serum urea, creatinine, and uric acid levels in comparison with the NC group. The STD group showed a significantly ($p \leq 0.05$) decreased urea, creatinine, and uric acid levels in comparison with the PC group. The FCLE treatment group also showed significantly ($p \leq 0.05$) reduced levels of urea, creatinine, and uric acid compared to the PC group, as illustrated in Figure 6.

Histopathological Analysis: Histopathological evaluation was performed to examine structural alterations in cardiac and aortic tissues. The experimental groups were the same as those described in our previous study (Khan *et al.,* 2025), which presented histopathology at 40X magnification, whereas the current images are displayed at 10X magnification. Histopathological analysis of heart tissue revealed well-organized cardiomyocyte architecture in the NC group, characterized by intact myocardial fibers, clear cellular boundaries, and distinct fibrillar bands indicative of healthy cardiac tissue (Figure 7A). In contrast, the PC group showed significant myocardial damage, evident from extensive infiltration of inflammatory cells, loss of

normal cellular demarcation, and disruption of myocardial fibers that are consistent with oxidative stress-induced injury in the infarcted myocardium (Figure 7B). The STD group demonstrated notable improvement in myocardial structure, with restoration of clearer cardiomyocyte boundaries along with reduced but persistent oxidative damage (Figure 7C). The FCLE treatment group exhibited marked attenuation of myocardial injury with reduced immune cell infiltration and ROS-mediated cellular damage, highlighting the FCLE antioxidant and anti-inflammatory properties (Figure 7D).

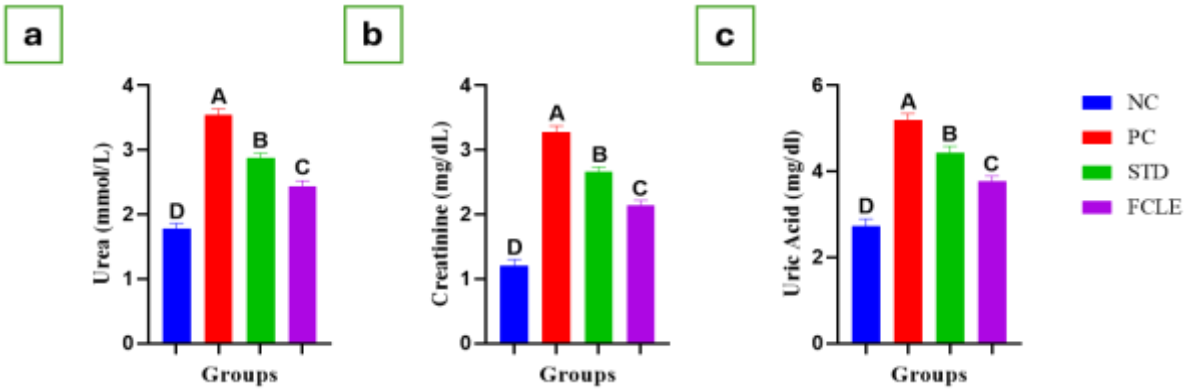

Figure 6 (a). Serum urea level in mmol/L (b). Serum creatinine level in mg/dL (c). Serum uric acid level in mg/dL across different experimental groups. The means bearing different superscripts (A, B, C, D) exhibit statistically significant differences at the threshold of p≤0.05.

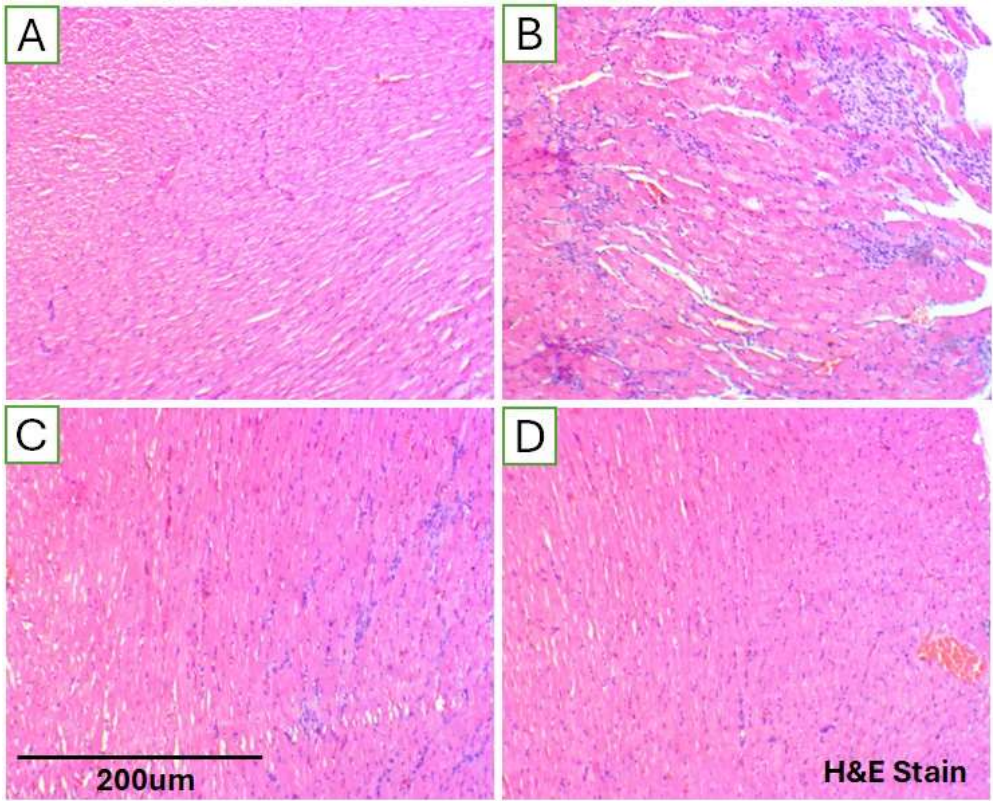

Figure 7. Representative photomicrographs of H&E-stained heart sections at 10X (200µm scale bar) across different experimental groups. (A). The NC group shows intact myocardial fibers and clear cellular boundaries (B). The PC group displays immune cell infiltration and disrupted myocardial architecture (C). The STD group shows partial recovery with reduced inflammation (D). The FCLE treatment group demonstrates significant improvement with restored cardiomyocyte integrity and decreased immune cell infiltration, highlighting its antioxidant and anti-inflammatory effects.

Histopathological analysis of aortic tissue revealed a normal aortic vascular layer with preserved endothelial lining and intact muscular arrangement in the NC group (Figure 8A). In the PC group, significant oxidative damage manifested irregular endothelial surface, medial thickening, along with marked immune cell infiltration (Figure 8B). The STD group showed partial restoration of aortic tissue structure and reduced inflammation with persistent damage of the tunica adventitia (Figure 8C). The FCLE treatment group exhibited substantial improvement with normalization of vessel wall thickness, diminished immune cell infiltration, and minimal oxidative damage, reflecting the antioxidant potential of FCLE (Figure 8D).

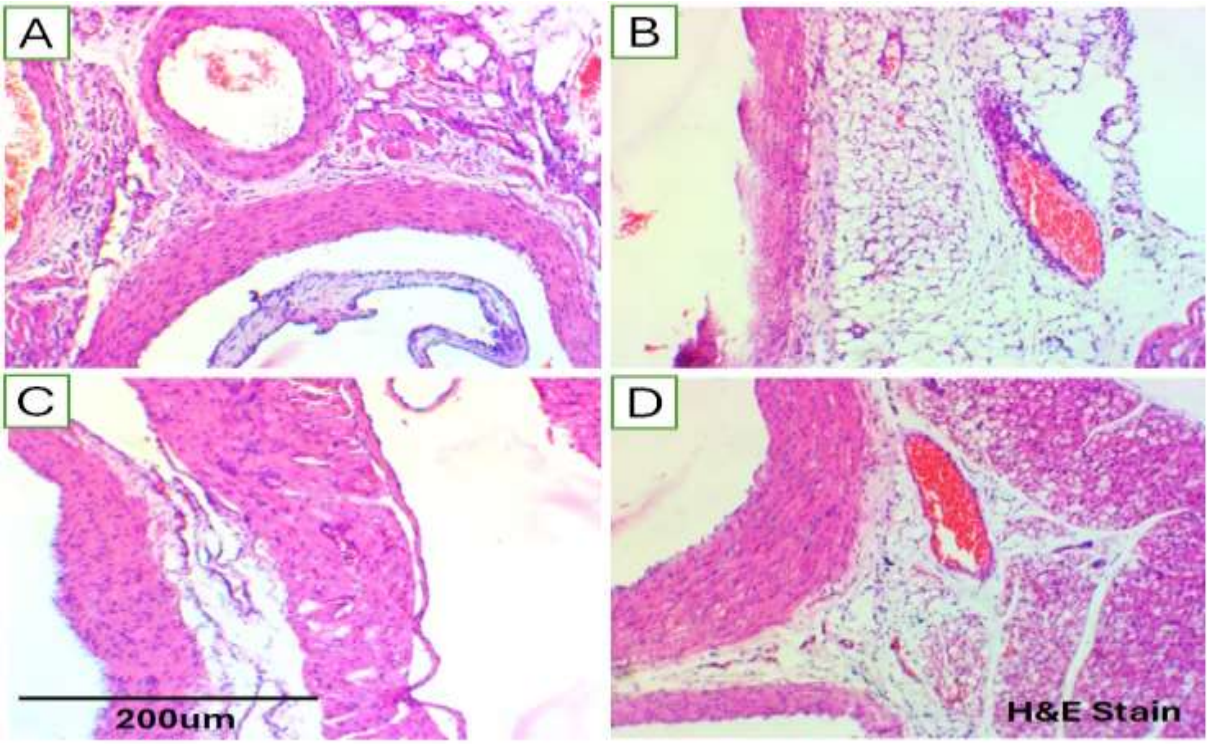

Figure 8. Representative photomicrographs of H&E-stained aorta sections at 10X (200µm scale bar) across different experimental groups. (A). The NC group showed a normal aortic vascular layer with preserved endothelial lining and muscular arrangement (B). The PC group exhibited an irregular endothelial surface with immune cell infiltration due to oxidative damage (C). The STD group showed partially improved tissue structure, but slight damage in the adventitia remained (D). The FCLE treatment group showed marked recovery with minimal oxidative damage, indicating its antioxidant protective effect.

DISCUSSION

FC contains a diverse range of phytochemicals, including flavonoids, phenolics, triterpenoids, coumarins, and phytosterols that collectively exert potent antioxidant and anti-inflammatory effects on oxidative stress-related conditions like myocardial infarction (Fazel *et al*., 2024). These compounds scavenge ROS and enhance endogenous antioxidant defenses, thereby mitigating oxidative damage to lipids, proteins, and DNA (Tikent *et al*., 2024; Vemula *et al*., 2024). The antioxidant activity of FC bioactive compounds has been demonstrated by a reduction in malondialdehyde level and an increase in enzymes like superoxide dismutase and catalase, contributing to the protection of mitochondrial function (Saghazadeh, 2023; Alawfi, 2025). Moreover, FC phytochemicals inhibit oxidative stress-induced inflammatory signaling pathways, including NF-κB and proinflammatory cytokines (TNF-α and IL-6), which are critical in the progression of tissue injury and remodeling (Rezagholizadeh *et al*., 2022; Altun *et al*., 2025). Studies have also highlighted that FC modulates mitochondrial membrane integrity and the apoptotic pathways induced by oxidative stress (Fazel *et al*., 2024). Furthermore, intracellular signaling pathways such as MAPK and PI3K/Akt are regulated by these FC phytochemical compounds, supporting cell survival and repair mechanisms under oxidative insult (Saghazadeh, 2023).

Natriuretic peptides are evaluated as the standard indicators for the diagnosis and prognosis of heart failure (Gruson *et al*., 2024). Research offers valuable insights into the regulation and secretion of B-type natriuretic peptide (BNP) in response to the stress

the heart experiences due to myocardial infarction, heart failure, and hypertension (Prajapati and Shah, 2024). Elevated levels of BNP indicate myocardial dysfunction in the PC group. Atrial cardiomyocytes release a hormone called atrial natriuretic peptide (ANP) in response to increased volume and membrane stress (Van Kimmenade and Januzzi, 2012). Ventricular cardiomyocytes also contribute to the release of ANP during heart failure (Magnussen and Blankenberg, 2018). The FCLE flavonoid content likely scavenges free radicals, preventing lipid peroxidation and stabilizing cardiac membranes (Fazel *et al.*, 2024). The normalization of both peptides in FCLE treatment groups suggests cardio protection.

Elevated TOS levels in the PC group reflect increased reactive oxygen species (ROS) production from ischemic myocardium and neutrophil activation, driving lipid peroxidation and cellular damage (Bashar and Akhter, 2014). The FCLE treatment group showed increased levels of TAC, aligning with its flavonoid content, neutralizing ROS, mirroring findings where enhanced antioxidant capacity reduces infarct size by stabilizing cardiac membranes (Frydrychowski *et al.*, 2022). The FCLE suppresses hydroxyl radical generation more effectively in conjunction with concurrent TOS reduction by potentially interrupting the ROS-inflammatory cascade (Aksoy *et al.*, 2022).

The FCLE treatment shows reduced AST and ALT levels, reflecting its cardioprotective mechanisms, reducing myocardial ischemia, as AST elevation in MI primarily originates from cardiac tissue damage (Ndrepepa, 2021; Thono *et al.,* 2023). The FCLE treatment shows reduced ALP levels, indicating reduced systemic oxidative stress, consistent with ALP's role in vascular calcification and cardiovascular mortality (Dinh Chien *et al.*, 2024). The parallel AST and ALT reduction mirrors findings where enzyme normalization correlates with infarct size reduction (Ndrepepa, 2021), suggesting FCLE preserves sarcolemma integrity in cardiomyocytes. Serum bilirubin levels often rise after myocardial infarction due to oxidative stress and impaired hepatic perfusion, and higher levels are linked to increased risk of adverse cardiac events (Shen *et al.*, 2019). FCLE treatment lowering bilirubin suggests reduced oxidative injury and improved cardiac function.

Myocardial infarction (MI) often leads to compromised renal function due to reduced cardiac output and subsequent renal hypoperfusion, resulting in elevated serum creatinine and urea levels, which are markers of impaired glomerular filtration rate (GFR) and renal injury (Rigattieri *et al.*, 2024). FCLE treatment significantly normalized serum creatinine, urea, and uric acid levels, suggesting improved renal perfusion and antioxidant effects that mitigate oxidative damage and inflammation in renal tissues. These findings align with previous reports where antioxidant-rich plant extracts reduced renal biomarkers and preserved kidney function in ischemic models (Zhang *et al.*, 2023).

This study lacks detailed molecular mechanism analysis of key oxidative stress and inflammatory pathways; however, these investigations are currently ongoing and will be reported in forthcoming publications.

Conclusion: FCLE confers significant cardioprotective effects in a rat model of high-fat diet coupled with isoproterenol-induced myocardial infarction. FCLE treatment improved cardiac biomarkers (BNP, ANP), restored oxidative balance (TAC, TOS), and normalized hepatic, renal, and systemic biochemical markers compared to the positive control group. These findings highlight FCLE's potential as a therapeutic agent for myocardial infarction and support further investigation into its clinical applications.

Conflict of Interest: The Authors declare no conflict of interest.

Authors' Contribution Statements: NUK executed the research, whereas SUH, BA, and SU conceived the idea and supervised the work.

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