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CURCUMIN AND ELLAGIC ACID ATTENUATE ISOPROTERENOL-INDUCED MYOCARDIAL INJURY IN RATS

Varsha Patwekar[1*], Vikas Rajurkar[2]

[1,2]Dr Vedprakash Patil pharmacy college, Georai Tanda, Chhatrapati Sambhaji Nagar – 431105, Maharashtra, India
*Corresponding Author: Varsha Patwekar

ABSTRACT
Oxidative stress-induced myocardial injury is a significant contributor to cardiovascular mortality and morbidity, prompting increasing interest in natural compounds with cardioprotective potential. Curcumin and ellagic acid are polyphenolic phytochemicals acknowledged for having strong antioxidant properties and cytoprotective properties. The present investigation assessed the protective effects of curcumin and ellagic acid, given both separately and in combination, against isoproterenol-induced myocardial injury in Wistar rats. Seven experimental groups—normal control, illness control, standard medication (gemfibrozil), and treatment groups receiving curcumin and ellagic acid—were randomly assigned to the animals. Test compounds were administered orally for 30 days, followed by subcutaneous administration of isoproterenol on days 29 and 30 to induce myocardial injury. Cardioprotective efficacy was evaluated by measuring serum creatine phosphokinase (CPK), Troponin-I, oxidative stress markers including reduced glutathione (GSH), lipid peroxidation (LPO), catalase (CAT), and superoxide dismutase (SOD), together with histopathological examination of myocardial tissue. Isoproterenol administration markedly increased serum CPK, Troponin-I, and LPO levels while reducing SOD, CAT, and GSH activities, accompanied by pronounced myocardial histopathological damage. Treatment with curcumin and ellagic acid significantly attenuated these biochemical and histological alterations, indicating protection against oxidative stress-induced cardiac injury. The combination treatment generally produced greater improvement than the individual treatments by restoring antioxidant status and preserving myocardial architecture. Overall, the findings demonstrate that rats' cardiac damage caused by isoproterenol is successfully mitigated by curcumin and ellagic acid. and support their potential for further investigation as natural therapeutic agents for myocardial protection.

KEYWORDS: Ellagic acid, isoproterenol, curcumin, myocardial damage, and oxidative stress.

INTRODUCTION

Cardiovascular diseases (CVDs) are still the single most important cause of death globally and myocardial infarction (MI) is a significant contributor to cardiovascular deaths and long-term disability. Even with the advent of pharmacologic and interventional treatments, the occurrence of myocardial injury and its complications still represent a major clinical and socioeconomic burden. Therefore, a search for safe and effective cardioprotective agents that could help minimize myocardial damage and enhance cardiac function is gaining interest (Najjar & Feresin, 2021). Plant-derived antioxidants have been of great interest in recent years due to the ability to regulate both oxidative stress and several molecular mechanisms known to be involved in myocardial injury (Alam et al., 2026).

Isoproterenol-induced myocardial injury is one of the most accepted experimental injury models to investigate cardioprotective interventions. The synthetic β-adrenergic agonist isoproterenol has been shown to cause myocardial damage, which includes excessive oxidative stress, calcium overload, lipid peroxidation (LPO) and cardiomyocyte necrosis, and therefore mimics several pathological features of human myocardial infarction. This model has thus emerged as a good platform for testing the possible cardioprotective compounds (Boarescu et al., 2019a). Other studies have also shown the potential of curcumin in reducing myocardial damage by decreasing the biochemical markers, oxidative stress and maintaining the myocardial architecture in experimental models of myocardial damage (Boarescu et al., 2019b).

Reactive oxygen species (ROS) production contributes to the progression of myocardial injury, and oxidative stress is a key factor involved.Excessive ROS production is a key factor in the progression of damage to the heart, through membrane LPO, mitochondrial dysfunction, and cellular damage. Superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) are examples of the endogenous antioxidant enzyme system is the main defense system against oxidative damage, whereas LPO is an indicator of oxidative damage of membranes. Serum cardiac biomarkers like creatine phosphokinase (CPK) and Troponin-I, which are well known markers of myocardial cell injury, are also routinely used for evaluating efficacy of cardioprotection (Komici et al., 2020; Ajzashokouhi et al., 2023).

Natural polyphenols' cytoprotective, anti-inflammatory, and antioxidant properties have thus come into the spotlight as potential cardioprotective agents. Curcumin, the major bioactive compound of Curcuma longa has shown to possess remarkable cardioprotective effect in various experimental models. Similarly, ellagic acid is a natural polyphenol found in several fruits and nuts, that has been shown to be cardioprotective against experimental cardiotoxicity, via antioxidant and cardioprotective effects on the myocardium (Hemmati et al., 2018). It is also well established that the antioxidants

from plants has a beneficial role in cardiovascular health by controlling the oxidative stress and age-related cardiac dysfunction (Khoso et al., 2025).

Medicinal plants and polyphenol rich formulation have been proven to possess cardioprotective effects on isoproterenol induced myocardial injury in various studies (Ganapathy et al., 2020; Keihanian et al., 2021). Single phytochemicals and natural products have also proven to have positive effects such as reducing oxidative stress, maintaining mitochondrial function and limiting myocardial damage (Hosseini et al., 2023; Viswanadha et al., 2021; Sun et al., 2020). However, there has been a lack of studies which have directly compared the cardioprotective effect of ellagic acid and curcumin used alone and in combination against a battery of alterations in histopathology, oxidative stress indicators, and cardiac markers in the same experimental model.

Natural phenolic compounds have been the subject of much interest due to their effects on oxidative stress and inflammatory pathways involved in cardiovascular disorders (Saleem et al., 2022). Several phytochemicals also have been shown to exert cardioprotective effects against myocardial damage via antioxidant and cytoprotective mechanisms (Sangeethadevi et al., 2019; Mattera et al., 2017). Furthermore, bioactive compounds found in diet can affect epigenetic regulation and cardiovascular function, and it has been proposed that herbal medicines can act as ion channel modifiers, providing further therapeutic potential in CVDs (Evans & Ferguson, 2018; Rajizadeh et al., 2026). Therefore, the goal of this study was to investigate the cardioprotective effects of curcumin and ellagic acid in rats with myocardial damage caused by isoproterenol.

Research Objectives

1.To evaluate the effects of curcumin and ellagic acid on serum cardiac biomarkers (CPK and Troponin-I).
2.To assess the effects of curcumin and ellagic acid on oxidative stress markers (SOD, CAT, GSH, and LPO).
3.To examine the histopathological changes in myocardial tissue following treatment with curcumin and ellagic acid.

2. METHODOLOGY

2.1 Test Substances

Curcumin and ellagic acid were used as the test substances in the present study. The doses of curcumin were 300 mg/kg (during the experimental period) and 600 mg/kg and the doses of ellagic acid were 60 mg/kg and 80 mg/kg respectively; both compounds were in powdered form and purified water was used as vehicle for oral administration throughout the experimental period.

2.2 Experimental Animals

Total 54 healthy Wistar rats either sex (200-300 g) were purchased from LACSMI Biofarms Pvt. Ltd., Pune, India. The animals were housed in polypropylene cages with autoclaved corn-cob bedding under laboratory conditions (12:12 hour light-dark cycle, temperature of 20–23°C, and relative humidity of 30–70%). The rats were given unlimited access to filtered drinking water and a conventional laboratory pellet diet (VRK Nutritional Solutions, Sangli, India). Before the experiment began, each animal was given a week to get used to the facility.

2.3 Experimental Design

After acclimatization, forty-two rats were randomly alienated into seven groups, of which each group consisted of six animals, for the cardioprotective study. Group 1 was used as normal control without treatment and isoproterenol induction and was not treated. Group II acted as a disease control group and were given isoproterenol, which is an agent that causes myocardial injury. Group III was given the usual drug gemfibrozil. Group IV was fed curcumin (600 mg/kg) along with ellagic acid (80 mg/kg). Group V was given only curcumin (300 mg/kg) and Group VI was given curcumin (300 mg/kg) and ellagic acid (60 mg/kg). Group VII was fed only with ellagic acid (60 mg/kg). In accordance with OECD Guideline 423, twelve rats were employed for acute oral toxicity testing, with two groups of 6 animals receiving each of the test compounds.

2.4 Administration and Induction Protocol

The test substances and the standard drug were given orally by means of oral gavage for 30 consecutive days. On Day 29 and Day 30, myocardial injury was induced in Groups II-VII by the subcutaneous injection of isoproterenol (85 mg/kg) and under identical experimental conditions throughout the study, the normal control group did not receive isoproterenol.

2.5 Sample Collection and Biochemical Assessment

All animals were underwent mild anaesthesia at the conclusion of the experiment, and blood samples were taken via retroorbital plexus puncture. The composed blood was centrifuged and the serum was separated, which was then used for the estimation of cardiac biomarkers. Serum CPK was analysed by an appropriate biochemical assay and the absorbance read at 450 nm. The concentration of Troponin-I (a sensitive biomarker of myocardial injury) was determined by a sandwich enzyme-linked immunosorbent assay (ELISA), and 450 nm was used to measure the absorbance.

By estimating LPO, decreased GSH, CAT, and SOD, the degree of oxidative stress on the heart tissue was determined. The absorbance of the MBAR adduct at 535 nm was used to assess thiobarbituric acid-reactive compounds (TBARS), which were then expressed as nmol MDA/mg protein in order to calculate LPO. Estimation of reduced GSH levels was done by Ellman's reagent (DTNB) and The absorbance was given as μmol/g of tissue and measured at 412 nm. The breakdown of H_2O_2 at 240 nm was used to quantify CAT activity and SOD activity was estimated by following the inhibition of epinephrine auto-oxidation at 480 nm. Enzymes activities were given as units per milligram of protein.

2.6 Toxicity and Safety Evaluation
Acute oral toxicity tests were conducted as per OECD Guideline 423. To assess the safety and tolerability of the test compounds, animals were given the dose levels selected and observed for 14 days for changes in body weight, behaviour, clinical indicators of toxicity, death, and general health.

2.7 Histopathological Evaluation
Myocardial tissues were removed after the completion of the experimental protocol, washed in chilled normal saline and fixed for at least 24 hours in 10% neutral buffered formalin. The tissues were fixed in standard paraffin embedding method and cut in 4-5 micrometers by rotary microtome. Haematoxylin and eosin (H&E) was used to stain the sections and viewed at various magnifications using a light microscope. Histopathological examination involved cytoplasmic vacuolization, sarcolysis, nuclear changes, infiltration of inflammatory cells, myocardial necrosis, interstitial fibrosis and other structural changes. A semi-quantitative grading system was used for the evaluation of tissue injury.

2.8 Study Overview
The preclinical study entitled "Pharmacological and Phytochemical Evaluation of Cardioprotective Activity of Some Medicinal Plants" (Study No. SCI/RD/VL/CARDIO RAT/2024-25/38) was conducted at SCITESLA Pvt. Ltd., Navi Mumbai, India. The study was sponsored by Ms. Varsha Suresh Patwekar and supervised by Mr. Akshay Nagishe (M.Pharm), with quality oversight provided by Ms. Vaishnavi Wanve (M.Sc.) and final authorization by Dr. Vishnu Thakare (Ph.D.). The experimental work was carried out between 2 October and 3 December 2024.

2.9 Ethical Compliance
Every experiment was authorised by the Institutional Animal Ethics Committee (IAEC) and carried out in accordance with the rules of the Committee for Control and Supervision of Experiments on Animals (CPCSEA). The study was performed as per the standard operating procedure of SCITESLA Pvt. Ltd. and Good Laboratory Practice (GLP) guidelines.

2.10 Statistical Analysis
GraphPad Prism was used to examine the data, and the results were displayed as mean ± standard deviation (SD). The body weight data were analysed by two-way ANOVA and Bonferroni's post hoc test, while biochemical parameters were examined using Bonferroni's post hoc test and one-way ANOVA. A statistically significant value was defined as $p < 0.05$.

3. RESULTS
3.1 Acute Oral Toxicity Study
In accordance with OECD Guideline 423, the acute oral toxicity research was conducted to determine the safety profile of the test substances before the pharmacological study was conducted. After oral administration at two dose levels animals were observed for general health, behavioural changes, clinical indicators of toxicity, and mortality. Table 1 summarises the outcomes of the experiments.

Table 1. Acute Oral Toxicity Study

Ani mal No	Date for onset of toxicity at Dose employed			
	300 mg/kg I	300 mg/kg II	2000mg /kg I	2000mg /kg II
1	NA	-	-	-
2	NA	-	-	-
3	NA	-	-	-
4	-	NA	-	-
5	-	NA	-	-
6	-	NA	-	-
7	-	-	NA	-
8	-	-	NA	-
9	-	-	NA	-
10	-	-	-	NA
11	-	-	-	NA
12	-	-	-	NA

No deaths or clinically toxic signs related to the treatment were noted in all of the experimental animals at either dose level as shown in Table 1. No animal had any abnormal behavior and did not have any clinical manifestation during the observation period and all animals were healthy. The test substances proved to be well tolerated under the experimental conditions and the estimated oral LD_{50}, using OECD Guideline 423, was found to be >2000 mg/kg.

3.2 Curcumin and Ellagic Acid's Impact on Weight

To assess the changes among the different treatments, body weight was monitored for 28 days of the experiment. Data on all experimental groups were collected on Days 0, 7, 14, and 28. Throughout the study, weight gain was noted but was different for each group. The statistical analysis included a two-way ANOVA with Bonferroni's post hoc analysis. Figure 1 shows the variations in body weight visually.

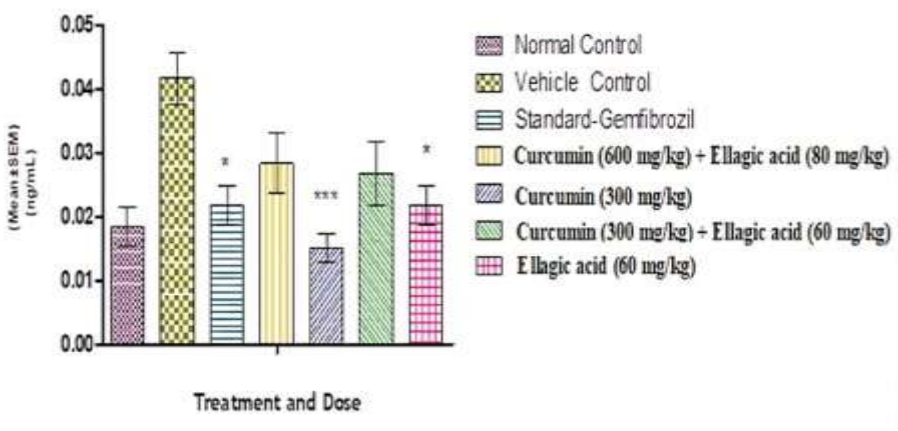

Figure 1. Body Weight impact in Rats during Pharmacological and Phytochemical Evaluation of Cardioprotective Activity

The body weight change of all the experimental groups during 28 days of the study are depicted in figure 1. The data are displayed as mean ± SD (n = 6), and two-way ANOVA and Bonferroni's post hoc test were used for statistical analysis.

3.3 Effect of Curcumin and Ellagic Acid on Serum CPK Levels

Serum CPK was evaluated in the experimental groups to evaluate myocardial damage at the conclusion of the treatment period. The serum CPK activity levels were found to be significantly different between the groups that received curcumin, ellagic acid, and a combination of curcumin and ellagic acid, as well as the normal control, vehicle control, and standard medication treated. The groups of vehicle control had the highest CPK activity while lower levels were observed in the treatment groups with ellagic acid alone having the lowest value among the tested treatments. The statistical analysis employed a one-way ANOVA and Bonferroni's post hoc test ($P < 0.0001$). The full quantitative results are displayed in Table 2.

Table 2 Curcumin's and ellagic acid's effects on Blood Serum CPK Levels during Pharmacological and Phytochemical Evaluation of Cardioprotective Activity in Rats

Treatment and Dose	(Mean±SD) (U/L)
Normal Control	154.17±3.87
Vehicle Control	175.33±3.88
Standard – Gemfibrozil	155.50±3.15
Curcumin (600 mg/kg) + Ellagic acid (80 mg/kg)	165.50±3.94
Curcumin (300 mg/kg)	156.00±3.22
Curcumin (300 mg/kg) + Ellagic acid (60 mg/kg)	162.67±2.07
Ellagic acid (60 mg/kg)	153.17±1.94

3.4 Effect of Curcumin and Ellagic Acid on Serum Troponin-I Levels

To assess myocardial injury after treatment in the experimental groups, serum levels of Troponin-I were measured. The concentration of Troponin-I was found to be different in the various treatment groups with the vehicle control being the highest, and comparatively lower in standard drug treated group and treatment groups. The treatment groups curcumin and ellagic acid alone had values similar to the normal control group. One-way ANOVA was used to analyse the data, and Bonferroni's post hoc test ($P < 0.0001$) came next. Figure 2 presents these results graphically.

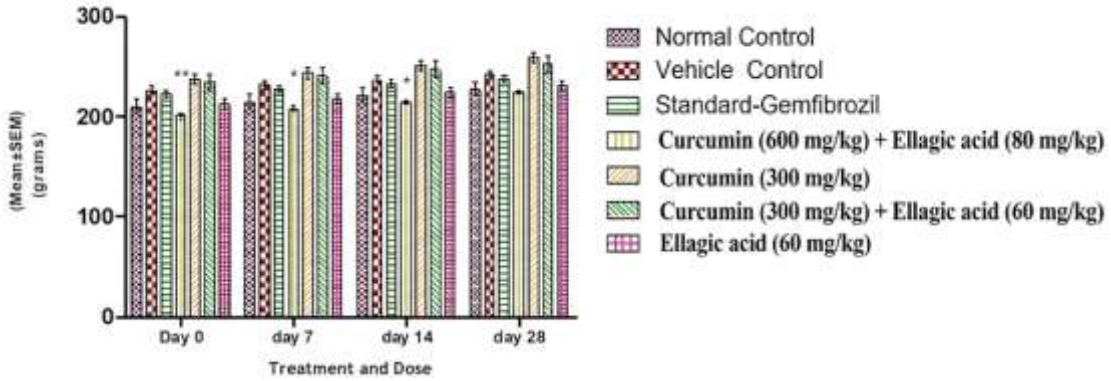

Figure 2. Curcumin and Ellagic Acid effects on Blood Serum Troponin-I Levels in Rats

The distribution of serum Troponin-I level within the groups is shown in Figure 2. One-way ANOVA with Bonferroni's post hoc analysis is used for statistical analysis, and values are shown as mean ± SD (n = 6).

3.5 Effect of Curcumin and Ellagic Acid on SOD Levels

SOD activity was found to evaluate antioxidant status of the experimental groups after treatment period. Significant differences in SOD activity were found among the normal control, vehicle control, standard drug-treated and treatment groups involving curcumin, ellagic acid and combination of both. SOD activity was lower in the vehicle control group than in the other groups and treatment groups with Ellagic acid alone demonstrated the highest enzyme activity among the treatments. Statistical analysis was conducted using a one-way ANOVA and Bonferroni's post hoc test ($P<0.0001$). Table 3 presents all of the quantitative findings.

Table 3. Effect of Curcumin and Ellagic Acid on SOD Levels in Rats

Treatment and Dose	(Mean±SD) (U/mg protein)
Normal Control	2.54±2.0
Vehicle Control	2.311±1.7
Standard – Gemfibrozil	3.44±2.4
Curcumin (600 mg/kg) + Ellagic acid (80 mg/kg)	2.53±1.5
Curcumin (300 mg/kg)	3.38±1.5
Curcumin (300 mg/kg) + Ellagic acid (60 mg/kg)	2.25±1.7
Ellagic acid (60 mg/kg)	4.8±2.8

3.6 Effect of Curcumin and Ellagic Acid on CAT Levels

After treatment, CAT activity was determined to assess the antioxidant enzyme response of the experimental groups. The enzyme activity of the CAT in the different experimental groups was found to be different, with the highest in the standard drug treated group. Moreover, higher activity of CAT was noted in animals given curcumin, ellagic acid and their combinations in comparison to the control groups, and this was different in each treatment. Bonferroni's post hoc test and one-way ANOVA ($P < 0.01$) were used for statistical analysis. These results are displayed graphically in Figure 3.

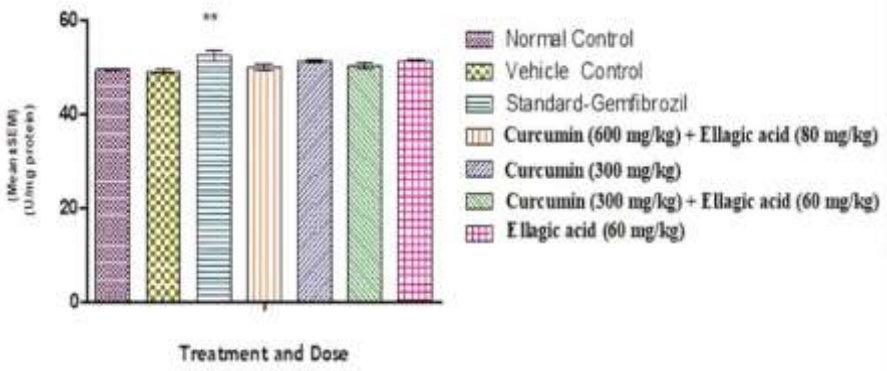

Figure 3. Effect of Curcumin and Ellagic Acid on CAT Levels in Rats

The distribution of CAT activity in the various experimental groups is shown in Figure 3. One-way ANOVA with Bonferroni's post hoc test was used for statistical analysis, and the values are mean ± SD (n = 6).

3.7 Effect of Curcumin and Ellagic Acid on Reduced GSH Levels

The level of reduced GSH was measured as an index of the endogenous antioxidant status of the experimental groups after treatment. The normal control, vehicle control, standard drug treated and treatment groups were found to have significant difference in GSH concentration between each group. Comparatively higher levels of GSH were seen in animals treated

with ellagic acid alone and with lower dose combination treatment and comparatively lesser levels in the higher dose combination treatment group. Bonferonni's post hoc test ($P < 0.0001$) was performed after one-way ANOVA. The total quantitative results are displayed in Table 4.

Table 4. Effect of Curcumin and Ellagic Acid on Reduced GSH Levels in Rats

Treatment and Dose	(Mean±SD) (µmol/L)
Normal Control	0.237±0.036
Vehicle Control	0.256±0.037
Standard – Gemfibrozil	0.276±0.051
Curcumin (600 mg/kg) + Ellagic acid (80 mg/kg)	0.227±0.030
Curcumin (300 mg/kg)	0.237±0.026
Curcumin (300 mg/kg) + Ellagic acid (60 mg/kg)	0.299±0.064
Ellagic acid (60 mg/kg)	0.301±0.089

3.8 Effect of Curcumin and Ellagic Acid on LPO Levels

To assess the level of oxidative damage in the experimental groups after treatment, the level of LPO was determined. The difference in the LPO level was found between the different groups, highest level was marked in vehicle control group while lower level was marked in the standard drug treated and treatment group. The lowest LPO level was found in the curcumin alone treated group and the intermediate levels were found in the combination treated groups among the phytochemical treatments (Figure 4).

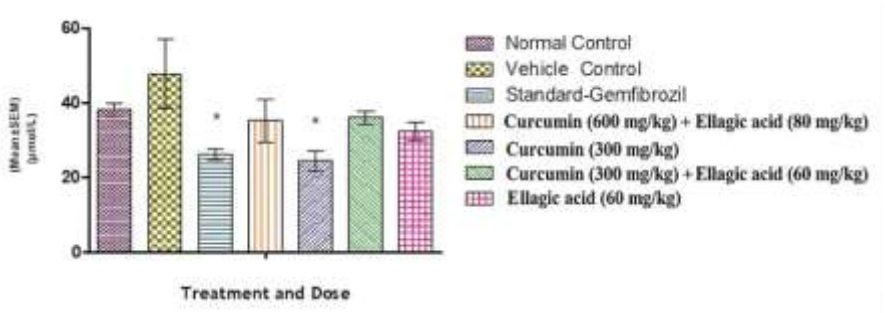

Figure 4. Effect of Curcumin and Ellagic Acid on LPO Levels in Rats

The distribution of levels of LPO is shown in Figure 4. Values are given as means ± SD (n = 6) and statistical analysis was carried out using one-way ANOVA with Bonferroni's post hoc test.

3.9 Histopathological Evaluation of Myocardial Tissue

The myocardial tissue was then subject to histopathological examination to evaluate the changes in the structure of myocardial tissue after myocardial injury induced by isoproterenol and therapy with curcumin, ellagic acid, its combination and standard drug. All experimental groups were analysed by microscopy of representative tissue sections, and myocardial injury was graded according to the histological changes observed. The detailed histopathological observation and injury grading of each experimental group is given in Table 5.

Table 5. Histopathological Observations of Myocardial Tissue

Group	Animal No.	Observations	Degree of Injury
G1 (Normal Control)	1	No abnormalities detected	0
	2	No abnormalities detected	0
G2 (Disease Control)	1	Papillary muscles and myocardium showed few to mild vacuolar changes of mild degree with minimal leucocytic infiltration.	1–2
	2	Papillary muscles and myocardium showed vacuolar changes of mild to moderate severity with mild to moderate leucocytic infiltration.	2–3
G3 Curcumin (600 mg/kg) + Ellagic acid (80	1	Mildly multifocal, mild vacuolation and loss of sarcoplasm. Minimal mononuclear cell infiltration and minimal scarring. Changes more prominent along the endocardium and papillary	2–3

mg/kg)		muscles.	
	2	Papillary muscles and nearby myocardium showed minimally multifocal vacuolation of minimal severity with loss of sarcoplasm. Minimal mononuclear cell infiltration.	1
G4 Curcumin (300 mg/kg)	1	Mildly multifocal vacuolar changes of minimal to mild severity with loss of sarcoplasm. Foci showed scarring and minimal mononuclear cell infiltration. Lesions noted along entire thickness of myocardium.	2
	2	Mildly multifocal, mild vacuolation and loss of sarcoplasm. Minimal mononuclear cell infiltration with mild scarring due to fibrous connective tissue deposition. Changes more prominent along endocardium and papillary muscles.	3
G5 Curcumin (300 mg/kg) + Ellagic acid (60 mg/kg)	1	Mildly multifocal, mild vacuolation and loss of sarcoplasm. Minimal mononuclear cell infiltration with mild scarring by fibrous connective tissue deposition. Changes more prominent along endocardium and papillary muscles.	2
	2	Mildly multifocal, mild vacuolation and loss of sarcoplasm. Minimal mononuclear cell infiltration with mild scarring by fibrous connective tissue deposition. Changes more prominent along endocardium and papillary muscles.	2–3
G6 Ellagic acid (60 mg/kg)	1	Mildly multifocal, mild vacuolation and loss of sarcoplasm. Minimal mononuclear cell infiltration with mild scarring by fibrous connective tissue deposition. Changes more prominent along endocardium and papillary muscles.	2
	2	Mildly multifocal, mild vacuolation and loss of sarcoplasm. Minimal mononuclear cell infiltration with mild scarring by fibrous connective tissue deposition. Changes more prominent along endocardium and papillary muscles.	2
G7 (Standard Drug)	1	Myocardium showed few small to medium-sized foci with vacuolar changes of moderate severity and loss of sarcoplasm. Minimal mononuclear infiltration.	1
	2	Myocardium showed few small to medium-sized foci with vacuolar changes of moderate severity and loss of sarcoplasm. Minimal mononuclear infiltration.	1–2

The different experimental groups showed histological differences. However, myocardial architecture was normal with no abnormalities found in the normal control group, while myocardial injury was found in the disease control group. Myocardial changes were observed in different degrees in animals receiving standard drug (curcumin), ellagic acid and combination of both the drugs, with minimum to moderate injury. The representative photomicrographs of these histopathological observations are shown in Figure 5 and Figure 6.

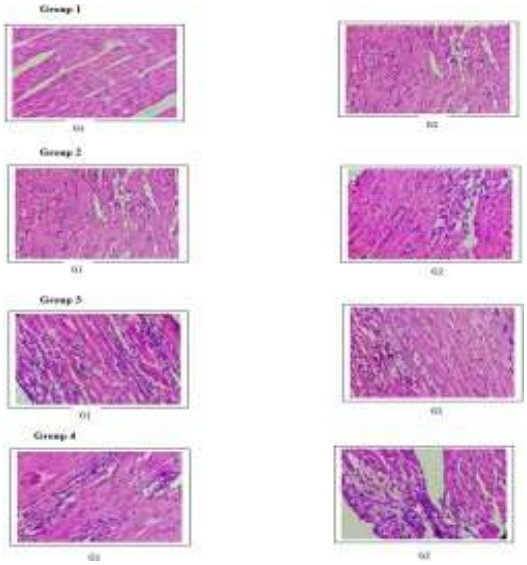

Figure 5. Histopathological Observations of Myocardial Tissue

The representative photomicrographs of myocardial tissue of different experimental groups are presented in Figure 5, showing the histological characteristics of myocardial tissue after various treatment groups. The images are related to the microscopic observations as summarised in Table 5.

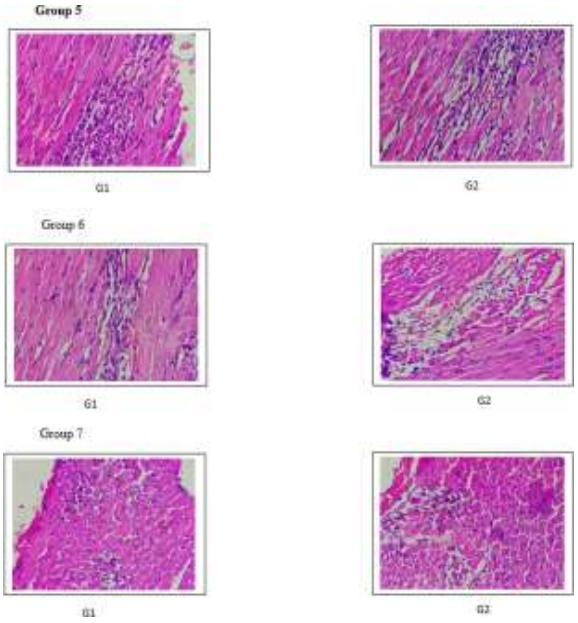

Figure 6. Histopathological Observations of Myocardial Tissue

Figure 6 shows other representative photomicrographs of myocardial tissue of the various experimental groups. The images are consistent with the histopathological features and myocardial injury grading in Table 5.

4. DISCUSSION

The current investigation outcomes indicated that curcumin and ellagic acid exhibited protective effect against isoproterenol-induced myocardial damage to rats through improvement of serum cardiac biomarker, oxidative stress parameters and histopathological architecture. When isoproterenol was administered, common characteristics of myocardial injury such as higher serum CPK, Troponin-I levels, higher LPO, decreased endogenous antioxidant levels and severe changes in the tissue. These pathological alterations were avoided by treatment with curcumin alone, ellagic acid alone, or together. This suggests that curcumin and ellagic acid play a preventive function in preserving cardiac integrity during oxidative stress.

The decrease in serum CPK and Troponin-I in the treated groups indicates a reduction in cardiomyocyte membrane damage and improvement in cell stability following phytochemical treatment. Similarly, the reduction in LPO levels and the recovery of antioxidant enzyme activity including SOD, CAT, and GSH suggest that the cardioprotective potential of curcumin and ellagic acid is closely linked to the improvement in antioxidant defense mechanisms. The results of the histopathology (HP) investigations were also in line with those of biochemical investigations, showing that the myocardial degeneration, inflammatory infiltration and tissue necrosis was less evident in treated animals than in disease control animals. All the above results suggest that the phytochemicals tested were effective in reducing the myocardial injury caused by isoproterenol.

The results obtained in the present investigation confirm the previous studies showing cardioprotective effect of natural products in experimental myocardial injury. Yoon et al. (2024) found that the herbal formulation TongGuanWan alleviated cardiac hypertrophy and fibrosis in experimental models through modulation of pathways related to myocardial injury. Similarly, Essa et al. (2026) displayed that the mix of polyphenols from the plants could help decrease cardiac injury by alleviating oxidative stress and metabolic disturbances in rats. The beneficial effects found in the present study are also similar to that of the review by Teng et al., (2022) which showed my protective effect of curcumin, a natural compound, on myocardial tissue on the basis of antioxidant and anti-inflammatory effects. Similar cardioprotective effects have been seen with Lepidium draba which showed that isoproterenol (Iso) induced myocardial infarction (MI) treated with Lepidium draba L. resulted in remarkable improvement in biochemical and histopathological parameters (Kahyaei et al., 2024). Moreover, Iqbal et al. (2019) demonstrated the ability of pitavastatin to reduce oxidative stress and inflammatory changes to prevent myocardial injury, highlighting the need to control oxidative damage as an important approach to therapy in experimental cardiomyopathy.

The results of this study confirm the therapeutic relevance of naturally occurring polyphenols as co-protective compounds in myocardial protection. Curcumin and ellagic acid could help decrease oxidative stress mediated cardiac injury by augmenting endogenous antioxidant defence, improving cardiac biomarkers and preserving myocardial histology. The findings discussed in the present study justify further research on phytochemicals as coadjuvants in the study of cardiovascular disease, as well as additional preclinical studies, concerning their use for protection against myocardial damage.

However, some caveats should be noted in this promising result. The study was carried out in an experimental rat model and the outcomes might not be immediately useful in a clinical setting. Biochemical, antioxidant and histopathological parameters were evaluated only and the identified cardioprotective effects' molecular mechanisms were not investigated. Further, the brief period of treatment and small sample size may limit the applicability of the results.
The chemical processes that underlie curcumin and ellagic acid's cardioprotective properties, such as their effects on inflammatory, apoptotic, and fibrotic signaling pathways, should be the focus of future studies. Prolonged preclinical studies, pharmacokinetic analyses and carefully designed clinical trials are also indicated to determine their clinical effectiveness, dosages and safety for use as a drug in CVDs.

5. CONCLUSION

Based on the current investigation, it was determined that curcumin and ellagic acid also have a substantial cardioprotective potential against myocardium damage caused by isoproterenol in mice. Isoproterenol administration induced extensive myocardial damage as reflected by the significant rise in serum cardiac markers, decrease in antioxidant enzymes, increase in LPO markers and significant histopathological changes in the myocardium. These pathological changes were effectively mitigated by curcumin, ellagic acid and their combination, thus revealing their protective effects on myocardial tissue. The noted drop in Troponin-I and serum CPK levels along with the rise in SOD, CAT, reduced GSH and the decrease in LPO indicates that the cardioprotective activity is closely associated to the maintenance of the oxidative balance and integrity of cells. Histopathological findings also confirmed the biochemical results, showing also a decreased myocardial degeneration, inflammatory infiltration and tissue damage in the treated animals. Of the interventions assessed, combination generally resulted in higher improvements than individual interventions, suggesting combination treatment is more effective at providing protection. Overall, the study's findings support the hypothesis that curcumin and ellagic acid have cardioprotective effects in isoproterenol-induced myocardial damage. The results suggest the therapeutic importance of these natural polyphenols for potential use in the alleviation of cardiac damage due to oxidative stress as adjunctive therapies. These findings warrant further mechanistic study and well-designed clinical study to validate the findings and determine their potentiality in preventing and managing CVDs.

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