Asian J Biol Life Sci., 2026; 15(2):419-428.
https://ajbls.com

Research Article

Therapeutic Potential of *Phyllanthus maderaspatensis* Extract on Isoproterenol-Induced Myocardial Infarction: An *in vivo* Examination

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ABSTRACT

Objectives: This study aims to assess the cardioprotective effect of *Phyllanthus maderaspatensis* leaf extract against isoproterenol-induced myocardial injury in rats. **Materials and Methods:** Rats were divided into groups and administered *P. maderaspatensis* extract at doses ranging from 100 to 200 mg/kg, subsequently subjected to isoproterenol-induced myocardial injury. Following treatment biochemical profile, cardiac bio markers and Histopathological investigation were performed, this research assessed the cardioprotective efficacy of *Phyllanthus maderaspatensis* leaf extract against Isoproterenol (ISO)-induced myocardial damage in experimental rats. **Results:** Body weight and haematological parameters, such as haemoglobin, Red Blood Cell (RBC), White Blood Cell (WBC), and platelet counts, remained consistent across all treated groups, demonstrating the extract's safety. ISO administration significantly increased serum lipid parameters, including total cholesterol, triglycerides, free fatty acids, phospholipids, LDL, and VLDL levels, while decreasing HDL levels. The lipid abnormalities were effectively normalised by treatment with *P. maderaspatensis* extract, especially at 200 mg/kg. Iron and ceruloplasmin, two markers of oxidative stress, were much higher in the ISO group than in the control group. However, after treatment with the extract, they were much lower. ISO inhibited antioxidant enzymes (SOD, CAT, GPx, and GST), but they were restored in a dose-dependent way. **Conclusion:** Membrane-bound ATPases (Na^+/K^+-ATPase, Ca^{2+}-ATPase, and Mg^{2+}-ATPase) exhibited enhanced activity following extract administration, suggesting the restoration of membrane integrity. Histopathological examinations of liver, kidney, and cardiac tissues indicated significant structural impairment in the ISO group, while extract-treated cohorts exhibited gradual recovery correlated with escalating doses. When the doses were higher, the structure of the tissue was almost the same as in the control group. These results indicate that *Phyllanthus maderaspatensis* exhibits considerable cardioprotective properties, presumably via antioxidant, lipid-lowering, and membrane-stabilizing mechanisms.

Keywords: Biomarkers, Cardiovascular, Histology, Myocardial, Phytomedicine.

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Received: 13-04-2026;
Revised: 28-05-2026;
Accepted: 03-07-2026.

INTRODUCTION

Myocardial Infarction (MI), characterized by the hypoxic state of cardiac tissue due to an imbalanced coronary blood flow compared to demand, is a leading cause of heart disease and mortality in men. MI results in ischemic damage to the myocardium and adversely affects the cardiomyocytes. Fixing damaged hearts in patients is challenging due to cardiomyocytes having a limited ability to regenerate following mitosis. Prolonged significant ischemia in chronic myocardial infarction ultimately leads to irreversible damage or death of heart muscle cells (Shanmugam *et al*., 2019). Specific Cardiovascular Diseases (CVDs), Particularly Ischemic Heart Disease (IHD) and hypertension, rank as the leading cause of death in developed nations, and their incidence is increasing globally (Yang *et al*., 2016). The genus *Phyllanthus* L. Traditional healers in India utilize whole plant extracts of *Phyllanthus maderaspatensis* for treating liver ailments. *Phyllanthus maderaspatensis* L. is an important medicinal plant within the *Phyllanthus* genus, prevalent in India, and used by traditional healers for treating liver disorders and other ailments (Akhtar *et al*., 2019). The plant is known for containing multiple pharmacologically relevant biomolecules, with their effectiveness validated by various biochemical and pharmacological studies (Sharma and Sheela, 2011). Londhe *et al*. (2012) attribute the hepatoprotective properties of *P. amarus* to compounds like

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DOI: 10.5530/ajbls.20260155

amariin and geraniin (types of ellagitannins), while phyllanthin and hypophyllanthin are proposed to have anti-inflammatory and anti-apoptotic effects. The hydro-alcoholic extract of *P. maderaspatensis* was found to contain rutin, catechin, gallic and ellagic acids, quercetin, and kaempferol (Kochumadhavan *et al.*, 2019). The hydro-alcoholic extract processed through repeated column chromatography yielded corilagin, an ellagitannin recognized for its anti-inflammatory and hepatoprotective effects. Rajeswari and Shabana Begum evaluated the hypolipidemic and hypoglycemic effects of ethanolic extracts from *P. maderaspatensis* leaves on rats induced with diabetes via Streptozotocin (STZ). The effect of ethanol extract of *P. maderaspatensis* was studied by Bommu *et al.* (2008) for its chemoprotective property on adriamycin-induced toxicity and oxidative stress in mice. Considering the increasing interest in the therapeutic potential of plant extracts and the well-established cardioprotective effects of various key compounds alongside the lack of literature addressing the assessment of cardioprotective characteristics of *P. maderaspatensis* was studied in this research.

MATERIALS AND METHODS

Plant material

P. maderaspatensis (voucher number: AUT/MCAS/176) was collected from Namakkal were dried in the shade, and then powdered with blender jar. The sample was extracted using a Soxhlet apparatus with ethanol for 72 hr. After that, the ethanolic extract was concentrated on a rotary vacuum drying machine under low pressure, and the weight of the yield was measured.

Animal used

Followed by the ethics committee (IAEC/MCAS/3/2022) approval all experimental procedures were strictly adhered with ethical guidelines. The cardioprotective activity was conducted on albino rats of both sexes (120-140 g), obtained from the central animal house facility of Jamia Hamdard, New Delhi. The rats were kept in a room with a 12-hr light/dark cycle at 25±2°C. They could eat a normal pellet diet and drink water whenever they wanted.

Treatments and dosing schedule

The experimental subjects were selected at random into five groups, each consisting of six rats (n=6). Before the experiment started, all of the animals had been acclimatised for 10 days. The study was carried out over 15 days according to a standard hepatoprotective protocol (Goyal *et al.*, 2015).

Group I

Rats treated with physiological saline (p.o.) alone with feed every for 15 days.

Group II

Rats were treated with physiological saline (p.o.) for 15 days and Isoproterenol (ISO) (100 mg/kg body weight, i.p.) was given on 4 and 15th day.

Group III

For 15 days, rats were treated with low dose of plant extract (100 mg/kg body weight, p.o.) once a day and ISO (100 mg/kg body weight, i.p.) on Days 14 and 15.

Group IV

Rats received plant extract (200 mg/kg body weight, p.o.) once daily for 15 days and ISO (100 mg/kg body weight, i.p.) on Days 14 and 15.

Group V

Rats were administrated with standard atorvastatin (1.0 mg/kg body weight, p.o.) once a day for 15 days. On Days 14 and 15, they were given ISO (100 mg/kg body weight, i.p.).

On Day 16, after the last ISO dose, the animals were put to sleep, starved for the night, and then killed. Blood samples were taken, and then they were spun at 3000 rpm for 10 min to separate the serum for biochemical testing. Liver tissues were cut out, washed with ice-cold saline, and then used for antioxidant tests and histopathological tests.

Serum analysis

On the 16th day of treatment period, all of the subject animals were put to sleep and killed. Blood was extracted from the heart, and their serum was isolated through centrifugation at 3000 rpm and 30°C for 15 min. After that, it was tested for different haematological and biochemical parameters, such as the serum lipids profile and lipoprotein content, using a semi-auto analyser and the Meril diagnostic kit (Azeez *et al.*, 2018).

Estimating Lipid Peroxidation Markers

The p-Phenylenediamine (PPD) oxidase method to figure out how much ceruloplasmin was in the serum. In short, 0.1 mL of serum was mixed with 2.0 mL of acetate buffer (0.1 M, pH 5.4) and then 1.0 mL of freshly made p-phenylenediamine solution was added. For 30 min, the reaction mixture was kept at 37°C, and then 0.1 mL of sodium azide was added to stop the reaction. Using a UV-visible spectrophotometer, we measured the absorbance of the developed colour at 530 nm against a reagent blank. Using a standard calibration curve, we measured the concentration of ceruloplasmin in mg/dL (Banjare *et al.*, 2017).

The Ferrozine colorimetric method (Goodwin, 1965) to find the serum iron level. In this method, 0.5 mL of serum was combined with 1.0 mL of acid buffer to liberate bound iron, and then 0.5 mL of a reducing agent (hydroxylamine hydrochloride) was added to

change Ferric Iron (Fe^{3+}) into Ferrous Iron (Fe^{2+}). After that, 1.0 mL of Ferrozine reagent was added, and the mixture was left at room temperature for 10 min so that a violet-colored complex could form. We measured the absorbance at 562 nm against a blank reagent. We used a standard iron solution to figure out the serum iron levels and wrote them down as µg/dL.

Heart homogenate enzymatic antioxidant analysis

Heart tissues were homogenised in KCl [10 mM] phosphate buffer (1.15%) with Ethylene-Diamine Tetraacetic Acid (EDTA pH 7.4) and centrifuged at 12000 rpm for 20 min. We used standard ELISA micro-plate assay kits to measure the levels of endogenous antioxidant enzymes like SOD, GPx, GRx, and GST in the clean supernatants of heart tissue extracts. The concentrations of SOD, GPx, GRx, and GST were quantified as units/mg of protein, nmol of NADPH oxidized/min/mg of protein, and nmol of CDNB conjugated/min/mg of protein, respectively. In short, 0.2 mL of the sample (digested with 0.1 N Sodium Hydroxide (NaOH)) was mixed with 2 mL of the working reagent (a mixture of 2% sodium carbonate, 0.1 N NaOH, 1.56% copper sulphate, and 2.37% sodium-potassium tartrate), and the reaction mixture was kept at room temperature for 10 min. After adding 1 N Folin-Ciocalteu's phenol reagent (0.2 mL), the mixture was left at room temperature for 30 min. Finally, the absorbance was checked at 660 nm. We used bovine serum albumin as a standard to figure out how much protein was in the samples.

Membrane-bound ATPases analsyis

The ATPase activities in the tissue homogenate by calculating toward amount of phosphorus was released from the test samples. Tris-HCl buffer (pH 7.4), NaCl, KCl, $MgCl_2$, and tissue homogenate were all in the reaction mixture. The reaction started when ATP was added and then it was left to sit at 37°C for 15 min. Trichloroacetic Acid (TCA) was added to stop the reaction. When Mg^{2+} ions are present, Mg^{2+}-ATPase breaks down ATP and releases inorganic phosphate, which can be measured using a spectrophotometer. The assay mixture was made up of tissue homogenate, $MgCl_2$, and Tris-HCl buffer. Adding ATP started the reaction, and it was left to sit at 37°C for 15 min. In the presence of calcium ions, Ca^{2+}-ATPase speeds up the breakdown of ATP, releasing inorganic phosphate, which can be measured colorimetrically. The reaction mixture, which had Tr/is-HCl buffer, $CaCl_2$, and tissue homogenate in it, was heated to 37°C for 15 min with ATP. TCA was added to stop the reaction, and the amount of inorganic phosphate that was released was measured at 620 nm.

Enzyme activity=µ moles of Pi liberated/mg protein × time

Histopathological Examination

After the animals were killed, the hearts were quickly cut open and washed with saline right away before being put in 10% formalin. After that, the fixed tissues were put in paraffin. After that, they cut serial sections that were 5 µm thick and stained them with Haematoxylin and Eosin (H & E). A Nikonphoto microscope was used to examine at the samples at 40x magnification.

RESULTS AND DISCUSSION

The initial evaluation of the impact of *Phyllanthus maderaspatensis* leaf extract on cardioprotection was conducted through the assessment of body weight variations in both control and treated rats (Table 1). The control group (G I) had a steady increase in body weight from 160.22±1.35 g to 175.25±1.55 g (Day 15). Group II (50 mg/kg) went from 160.34±1.22 g to 175.42±1.15 g. The values for Group III (100 mg/kg) were 160.51±1.53 and 175.49±1.28 g on Day 15. The body weight of Group IV (200 mg/kg) went up from 160.43±1.13 g to 175.61±1.65 g, which was the most weight gain of any group on Day 15. Group V (400 mg/kg) had a range of 160.67±1.52 to 175.39±1.66 g, and Group VI (800 mg/kg) had a range of 160.58±1.54 to 175.58±1.44 g at the same times. The results showed no statistically significant variations in body weight increase between the control and treated groups, despite minor variation. The gradual increase over all doses shows that the extract did not cause toxicity or metabolic problems that would slow growth. Giving *P. maderaspatensis* extract, even in higher doses (up to 800 mg/kg), is well tolerated and does not cause weight gain, which supports its safety during treatment (Kanala *et al*., 2025).

The levels of haemoglobin stayed the same in all groups, with group I having 11.56, group II having 11.39, group III having 11.63, group IV having 11.51, group V having 11.70, and group VI having 11.69 g/dL. RBC counts showed a small increase, with values of 5.12, 5.33, 5.50, 5.37, 5.41, and 5.77 $\times 10^6$/mcL from group I to VI as the doses went up. This suggests that erythropoietic function was still working. WBC counts stayed in the normal range, with values of 3.36, 3.70, 3.45, 3.68, 3.52, and 3.80 $\times 10^3$/mcL for groups I to VI. This means that there were no signs of inflammation or immunosuppression. Platelet counts were consistent across all groups, with values of 2.54, 2.84, 2.89, 2.77, 2.60, and 2.59 $\times 10^5$/µL from group I to VI, indicating no detrimental effect on thrombopoiesis. The haematological characteristics in all treatment groups were similar to those in the control group, with only minor differences and no dose-dependent toxicity (Table 2). The findings indicate that *P. maderaspatensis* extract does not induce any adverse alterations in haematological parameters, thereby supporting its safety during the treatment period (Regmi *et al*., 2025).

After administration to *P. maderaspatensis* extract, serum lipid profile levels were measured. For total cholesterol, the levels

were 73.11 (Control), 128.55 (ISO), 91.09 (100 mg/kg), 69.87 (200 mg/kg), and 71.50 mg/dL (Standard). The triglyceride levels were 150.12, 330.55, 221.40, 159.12, and 155.47 mg/dL. The levels of free fatty acids were 23.38, 60.18, 49.77, 30.23, and 26.51 mg/dL. The levels of phospholipids were measured at 10.66, 31.51, 20.74, 13.40, and 12.55 mg/dL (Table 3). ISO induction significantly disrupted lipid homeostasis, whereas treatment with *P. maderaspatensis* efficiently suppressed these alterations, especially around a dosage of 200 mg/kg, thereby demonstrating its substantial hypolipidemic and cardioprotective potential. The decrease in lipid parameters is in line with what Radhiga *et al.* (2012) found, which was that isoproterenol-induced conventional models showed strong hypolipidemic impacts.

Effect of serum lipoprotein profile

The effect of *P. maderaspatensis* extract on the analysis of serum lipoproteins (Table 4) showed the HDL cholesterol levels were 35.70, 19.22, 27.13, 32.55, and 34.23 mg/dL for Groups I to V, which is a big drop. The LDL cholesterol levels in Groups I to V were 25.66, 54.81, 30.16, 22.50, and 24.75 mg/dL, which is a big increase. In Group I to V, VLDL levels were 30.72, 65.41, 43.12, 36.67, and 32.90 mg/dL. This shows a big rise in the ISO group, followed by a drop that depends on the dose of the extract (Figure 1). *P. maderaspatensis* effectively reversed the ISO-induced disruption of lipoprotein balance, demonstrating significant antihyperlipidemic effects. The enhancement in lipoprotein levels aligns with the findings of Khalil *et al.* (2015), which illustrated a beneficial impact against isoproterenol-induced cardiovascular damage.

Effect of lipid peroxidation markers

The concentrations of lipid peroxidation markers demonstrated iron levels about 15.33, 69.40, 21.18, 17.59, and 14.22, and ceruloplasmin values as 12.61, 23.70, 16.43, 13.09, and 11.80 in Groups I to V. This means that the ISO group had a big increase, and then the levels went down with *P. maderaspatensis* extract (Figure 2). This decrease shows that oxidative damage is lessening at the cellular level. The effect may be due to the extract's ability to fight free radicals and act as an antioxidant. The decrease in lipid peroxidation markers noted in this study corresponds with the findings of Al-Numair *et al.* (2014), reinforcing the function of antioxidants in alleviating myocardial oxidative stress.

Effect of antioxidant enzymes

The ISO group had a significant drop in antioxidant enzymes in contrast to the control group. The levels of SOD, CAT, GPx, and GST were 121.70, 9.44, 45.63, and 14.48, respectively, in the control group. In the ISO-induced group, they dropped to 59.33, 2.87, 19.72, and 8.02. *P. maderaspatensis* extract gradually reversed this decrease, with values going up to 89.44, 6.61, 32.69, and 10.55 at 100 mg/kg and then to 104.33, 7.94, 41.20, and 12.67 at 200 mg/kg. The standard drug also brought enzyme levels back to 118.67, 8.89, 43.33, and 14.04, which shows that the antioxidant defence was able to recover (Figure 3). ISO induction significantly inhibited anti-inflammatory defence mechanisms, whereas *P. maderaspatensis* successfully recovered enzymatic antioxidant levels, underscoring its robust antioxidative and cardioprotective properties. The recovery of antioxidant enzyme concentrations found in this study is consistent with Asaikumar *et al.* (2019), corroborating the role of antioxidants in safeguarding against isoproterenol-induced myocardial injury.

Restorartion of cardiac ATPase activity by *P. maderaspatensis*

The membrane-bound ATPases Na^+K^+ ATPase, Ca^{2+} ATPase, and Mg^{2+} ATPase activity in cardiac tissue. The control group's

Table 1: Changes in body weight of control and induced rats during treatment with different dosages of ethanol extract of *P. maderaspatensis* leaves.

Groups	Dose (mg/kg b.wt)	Initial Body weight (g)	Day 5 (g)	Day 10 (g)	Day 15 (g)
G I	Control	160.22±1.35	164.31±1.44	169.34±1.28	175.25±1.55
G II	50	160.34±1.22	164.52±1.54	169.50±1.35	175.42±1.15
G III	100	160.51±1.53	164.49±1.35	169.55±1.14	175.49±1.28
G IV	200	160.43±1.13	164.62±1.48	169.74±1.34	175.61±1.65
G V	400	160.67±1.52	164.41±1.36	169.48±1.14	175.39±1.66
G VI	800	160.58±1.54	164.55±1.22	169.66±1.15	175.58±1.44

Table 2: Effect of ethanol extract of *P. maderaspatensis* leaves on hematological parameters.

Hematological parameters	Group I (Control)	Group II 50 mg/kg b.wt	Group III 100 mg/kg b.wt	Group IV 200 mg/kg b.wt	Group V 400 mg/kg b.wt	Group VI 800 mg/kg b.wt
Hemoglobin (g/dL)	11.56±0.05	11.39±0.08	11.63±0.05	11.51±0.06	11.70±0.07	11.69±0.06
RBC ($\times10^6$/mcL)	5.12±0.07	5.33±0.05	5.50±0.05	5.37±0.08	5.41±0.05	5.77±0.06
WBC ($\times10^3$/mcL)	3.36±0.05	3.70±0.07	3.45±0.06	3.68±0.08	3.52±0.06	3.80±0.06
PLT ($\times10^5$/❍L)	2.54±0.06	2.84±0.07	2.89±0.06	2.77±0.05	2.60±0.07	2.59±0.05

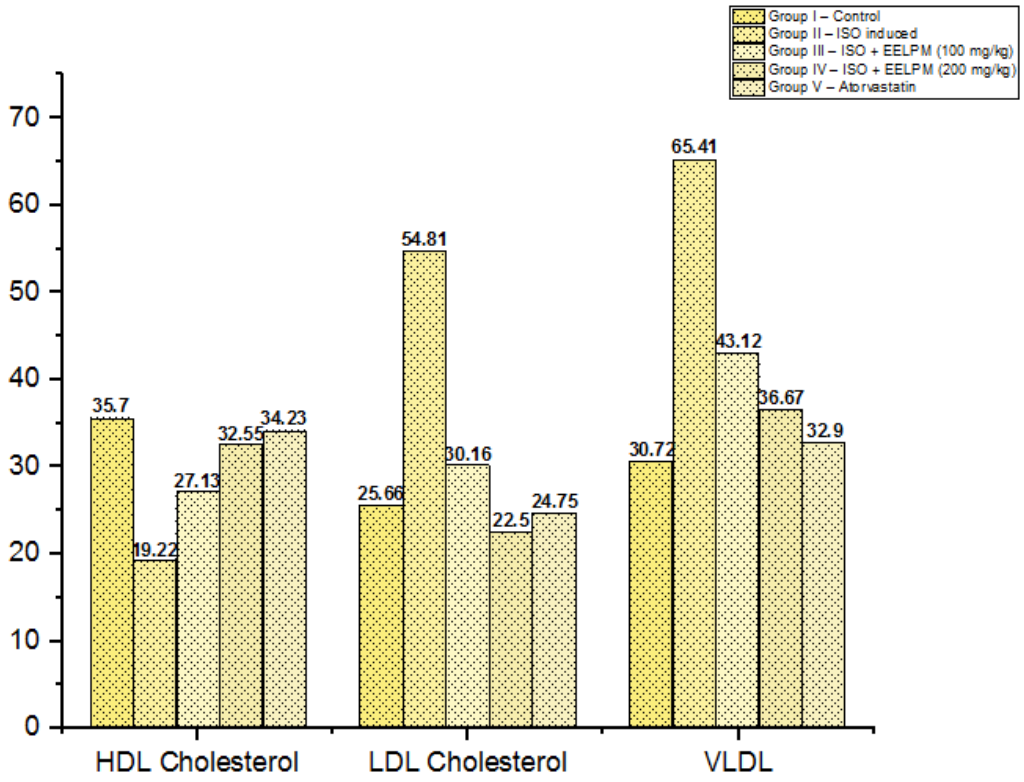

Figure 1: Serum lipoprotein profile in control and ISO induced rats.

Table 3: Effect of lipids present in serum of control and ISO induced rats

Groups	Cholesterol	Triglycerides (TG)	Free Fatty Acids (FFA)	Phospholipids
Group I- Control	73.11±6.61	150.12±7.20	23.38±1.51	10.66±0.81
Group II- ISO induced	128.55±8.90	330.55±9.05	60.18±2.05	31.51±1.58
Group III- ISO + EELPM (100 mg/kg b.wt)	91.09±7.44	221.40±8.33	49.77±1.55	20.74±1.22
Group IV- ISO + EELPM (200 mg/kg b.wt)	69.87±5.33	159.12±5.87	30.23±1.25	13.40±0.82
Group V- Atorvastatin (Standard)	71.50±5.49	155.47±5.05	26.51±1.02	12.55±0.60

ATPase activity were 0.71, 0.80, and 0.55; in the ISO-induced group, they were 0.32, 1.85, and 0.96. These values were 0.40, 1.44, and 0.70 at 100 mg/kg and 0.62, 1.08, and 0.62 at 200 mg/kg following exposure to *P. maderaspatensis* extract. Values of 0.65, 0.91, and 0.58 for the usual medication indicated a return to normal enzyme activity (Table 5). *P. maderaspatensis* successfully restored membrane enzyme function, indicating its protective role against cardiac membrane injury, while ISO induction disrupted ATPase activities. The analysis of ATPase activity is in line with Sukhov *et al.* (2024), underscoring the significance of preserving ion transport systems for heart function (Figure 4).

Hepatoprotective effect of *P. maderaspatensis*

Histopathological analysis of liver sections (Figure 5) showed that the control group (G I) had a healthy liver structure, with well-organised hepatocytes, an intact central vein, and no cellular degeneration. There were big changes in the histology of the ISO-induced group (G II), like hepatocellular degeneration, inflammatory cell infiltration, and changes in the shape of the liver. This suggests that the tissue was damaged. The extract-treated groups showed steady improvement as the dose was raised. Group III (100 mg/kg) showed some repair of the liver's structure and some cell death. Group IV (200 mg/kg) had hepatocytes that were almost normal, less inflammation, and better tissue organization. Groups V (400 mg/kg) and VI (800 mg/kg) had higher doses,

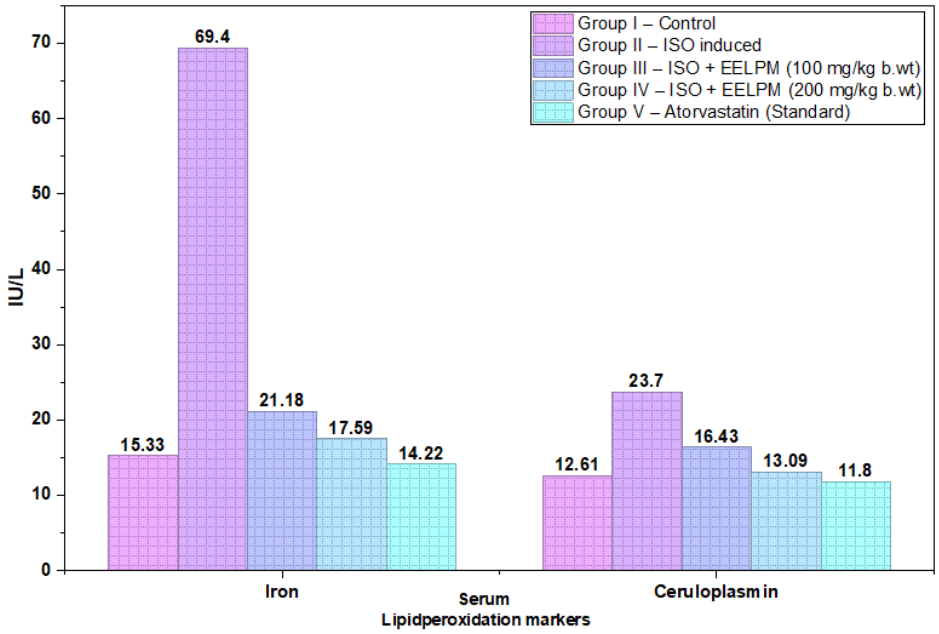

Figure 2: Effect of lipid peroxidation markers (Iron and Ceruloplasmin) in serum of ISO induced rats.

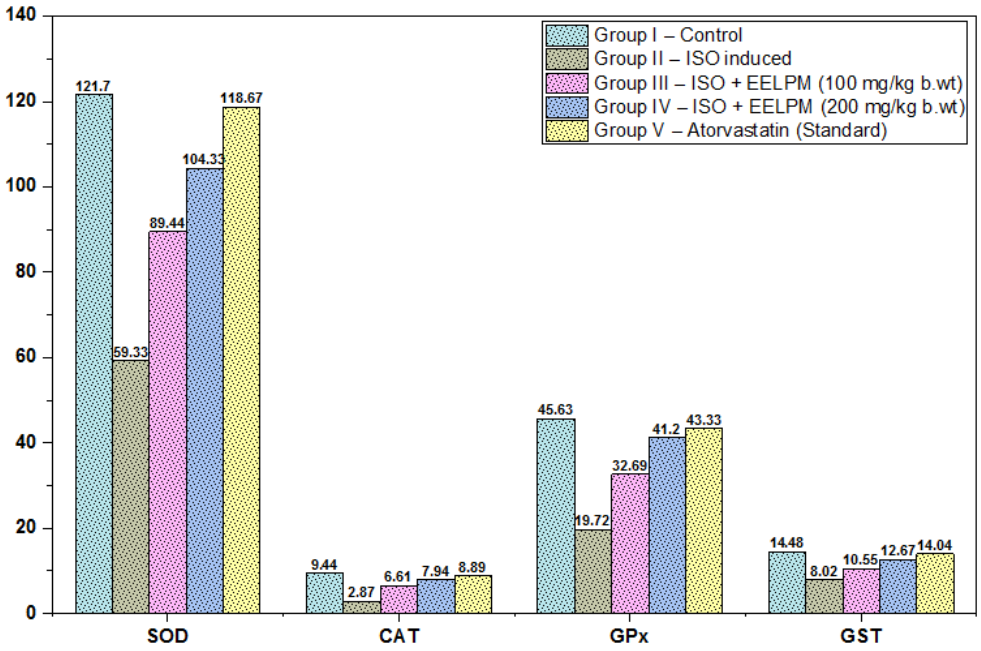

Figure 3: Effect of enzymatic antioxidants in ISO induced rats.

Table 4: Effect of lipoproteins present in serum of control and ISO induced rats.

Groups	HDL cholesterol	LDL cholesterol	VLDL
Group I-Control	35.70±1.55	25.66±1.85	30.72±1.47
Group II-ISO induced	19.22±0.87	54.81±2.54	65.41±2.55
Group III-ISO + EELPM (100 mg/kg b.wt)	27.13±1.21	30.16±1.90	43.12±2.03
Group IV-ISO + EELPM (200 mg/kg b.wt)	32.55±1.40	22.50±1.50	36.67±1.66
Group V-Atorvastatin (Standard)	34.23±1.45	24.75±1.55	32.90±1.50

Table 5: Effect of membrane bound ATPases such as Na^+K^+ ATPase, Mg^{2+} ATPase, Ca^{2+} ATPase were assayed in the heart homogenate of control and experimental animals

GROUPS	Na^+K^+ ATPase	Ca^{2+} ATPase	Mg^{2+} ATPase
Group I - Control	0.71±0.09	0.80±0.05	0.55±0.07
Group II - ISO induced	0.32±0.05	1.85±0.18	0.96±0.15
Group III - ISO + EELPM (100 mg/kg b.wt)	0.40±0.05	1.44±0.12	0.70±0.11
Group IV - ISO + EELPM (200 mg/kg b.wt)	0.62±0.06	1.08±0.09	0.62±0.08
Group V - Atorvastatin (Standard)	065±0.07	0.91±0.07	0.58±0.08

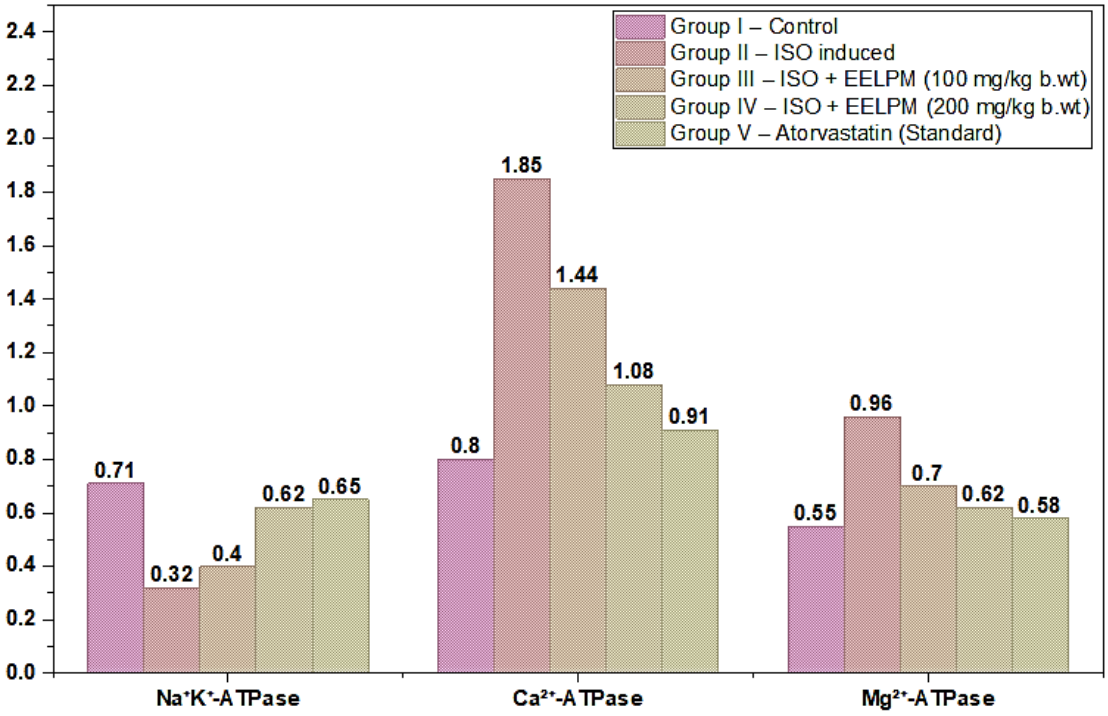

Figure 4: Effect of membrane bound ATPases such as Na^+K^+ ATPase, Mg^{2+} ATPase, Ca^{2+} ATPase were assayed in the heart homogenate of control and experimental animals.

but their liver architecture was still well-preserved and there was little to no degradation. The histological findings illustrate the protective effect of *P. maderaspatensis* extract against tissue damage by validating its significant reduction of ISO-induced liver injury in a dose-dependent fashion. The histological changes reported confirm the role of tissue healing in mitigating liver damage and align with the findings of Elwan *et al.* (2024).

Nephroprotective effect of *P. maderaspatensis*

The control group (G I) exhibited normal renal histology, characterised by intact glomeruli, a distinctly defined Bowman's capsule, and standard tubular architecture, as determined by histopathological examination of kidney sections (Figure 6). The ISO-induced group (G II) showed a lot of damage to the kidneys, such as glomerular shrinkage, tubular degeneration, and the infiltration of inflammatory cells. This suggests that the kidneys were not working properly. Extract-treated groups exhibited structural healing in a dose-dependent manner. Group III (100 mg/kg) showed some repair of the glomerular structure and some damage to the tubular structure. Group IV (200 mg/kg) exhibited better-preserved tubules and an enhanced kidney morphology with reduced cellular damage. The higher doses in Group V (400 mg/kg) and Group VI (800 mg/kg) were very similar to the control group.

Their renal histology was almost normal, their glomeruli were not damaged, and there were only a few signs of degeneration over time. It also suggests a protective effect that depends on the dose, with higher doses showing almost complete restoration of kidney structure. This protective effect may be due to the extract's ability to fight free radicals and stabilise membranes. The enhancements in renal histopathology align with the findings of Al-Rikabi *et al.* (2021), which underscore the role of protective measures in reducing tissue damage.

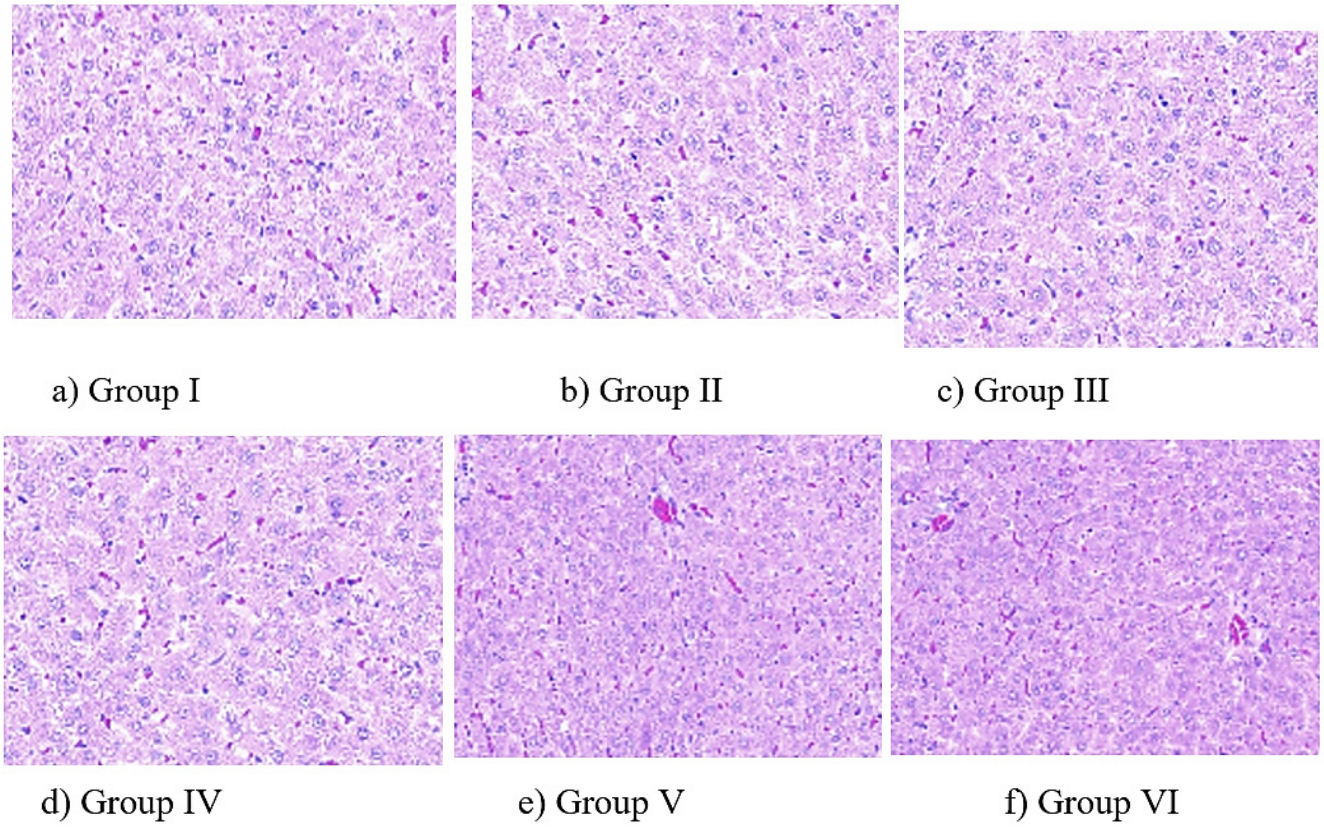

Figure 5: Acute toxicity Histopathological examinations of liver of control and EELPM treated.

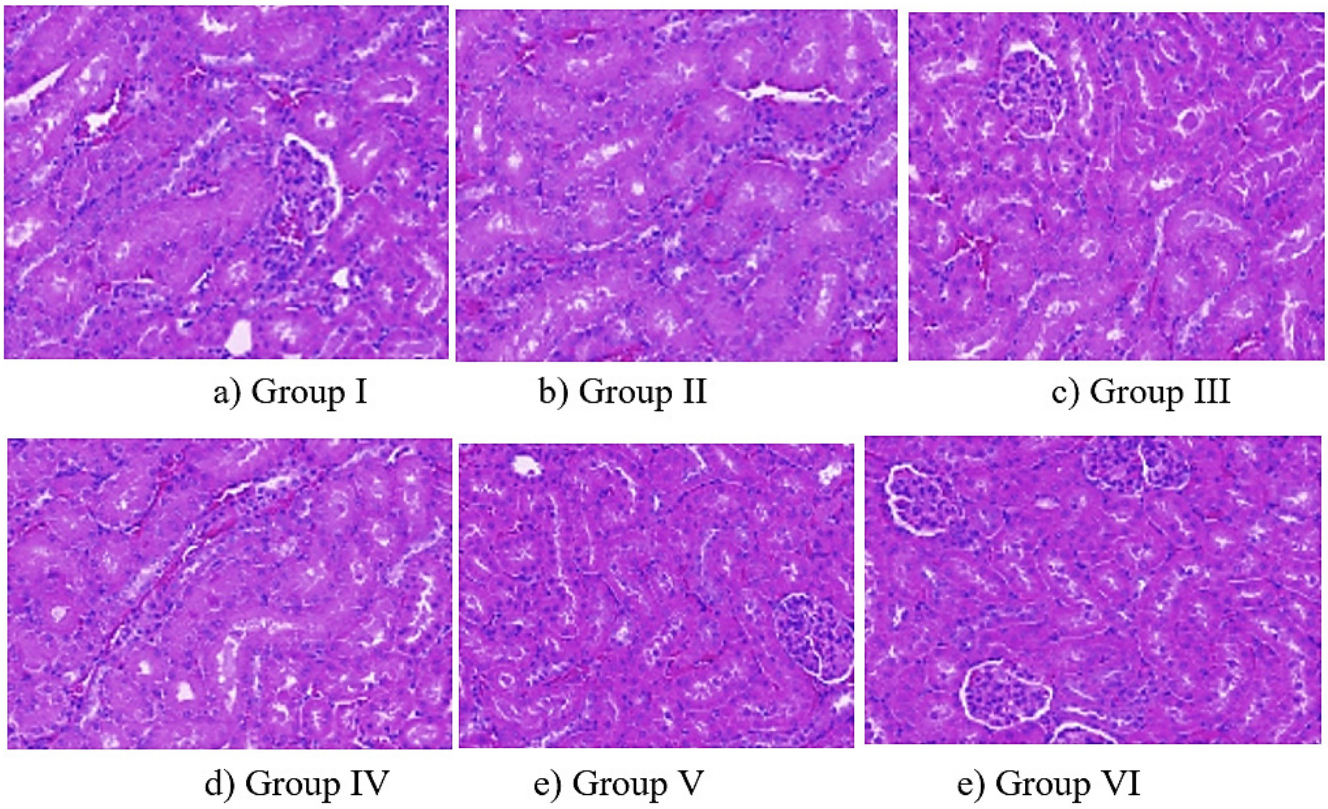

Figure 6: Histopathological examinations of kidney of control and EELPM treated.

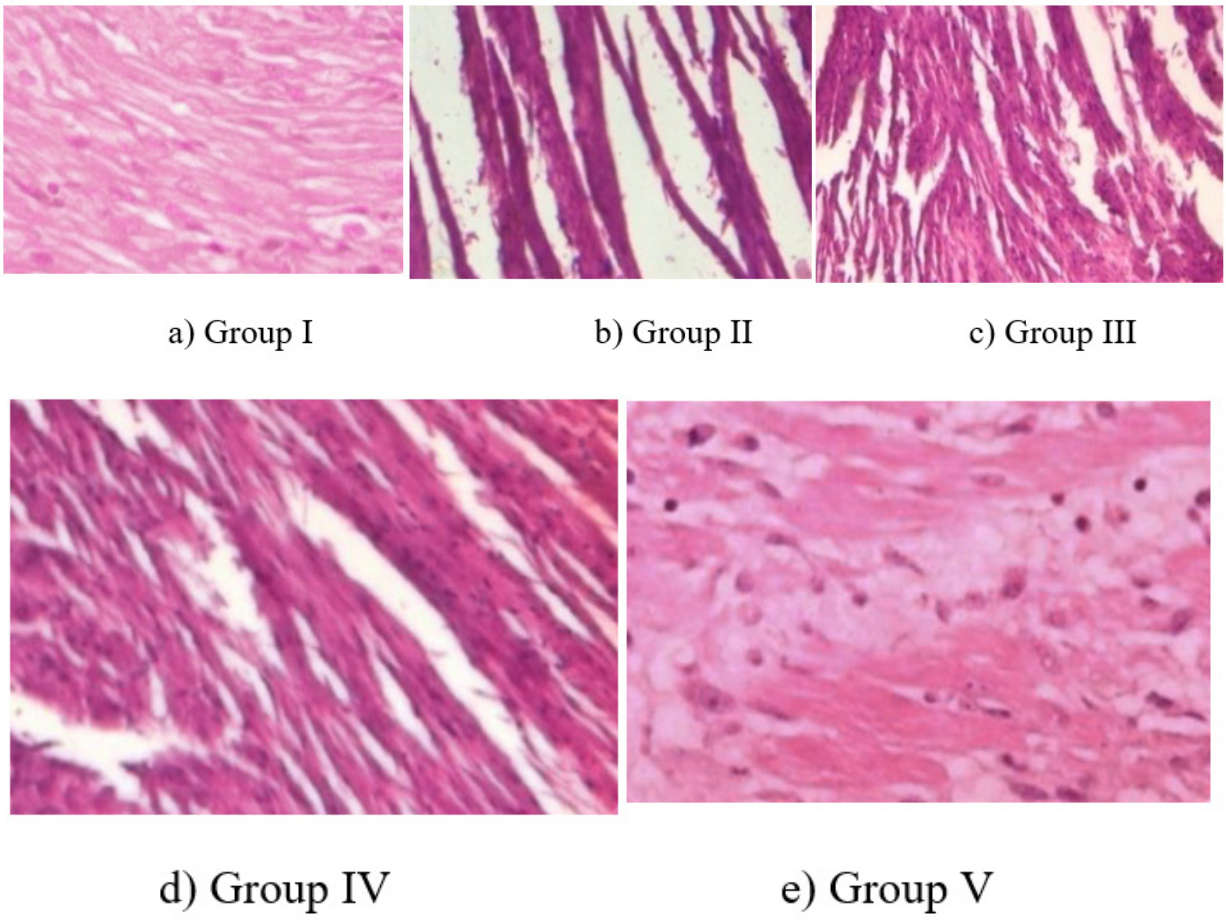

Figure 7: Effect of EELPM on ISO induced histopathological changes in heart tissue.

Cardioprotective activity of *P. maderaspatensis*

Histopathological analysis of heart tissue (Figure 7) showed that the control group (G I) had normal myocardial morphology. This means that the cardiac muscle fibres were well-organised, the nuclei were intact, and there were no structural problems. Cardiac injury was apparent in the ISO-induced group (G II), which exhibited significant myocardial damage, characterised by compromised muscle fibres, cellular degeneration, and inflammatory infiltration. The groups that were given the extract showed an improvement in myocardial structure that depended on the dose. Group III (100 mg/kg) exhibited partial preservation of muscle fibre organization alongside significant myocardial damage. Group IV (200 mg/kg) exhibited superior cardiac fibre alignment and myocardial morphology with reduced degeneration. The standard drug group (G V, atorvastatin) exhibited minimal pathological alterations and an almost normal cardiac structure with well-preserved fibres. It also shows that the integrity of the heart muscle is better preserved as the dose levels go up. This benefit may be due to the extract's antioxidant and membrane-stabilizing properties, which reduce damage to the heart muscle. The cardioprotective results of this study corroborate the function of protective agents in mitigating isoproterenol-induced myocardial injury, aligning with the findings of Hareeri *et al.* (2023).

CONCLUSION

The current research indicates that *Phyllanthus maderaspatensis* leaf extract effectively safeguards rats' hearts against ISO-induced cardiac damage. The extract is considered safe as it showed no harmful effects on blood parameters or body weight. It enhanced lipid profiles, diminished oxidative stress, bolstered antioxidant defense mechanisms, and reinstated membrane-bound enzyme activity in a dose-dependent manner. By maintaining the structural integrity of cardiac, liver, and kidney tissues, histopathological findings further reinforced its protective function. Among all the doses examined, the 200 mg/kg dosage provided the most significant therapeutic advantage, similar to the standard treatment. These results indicate *P. maderaspatensis* as a possible natural cardioprotective agent that could be used to avert cardiac problems related to oxidative stress. Further research is necessary to identify active components and clarify specific chemical processes.

ACKNOWLEDGEMENT

None.

ABBREVIATIONS

ISO: Isoproterenol; **MI:** Myocardial Infarction; **CVDs:** Cardiovascular diseases; **IHD:** Ischemic heart disease; **STZ:** Streptozotocin; **p.o.:** per os (by mouth); **i.p.:** intraperitoneal; **RBC:** Red blood cell; **WBC:** White Blood Cell; PLT: Platelet; **LDL:** Low-density lipoprotein; **VLDL:** Very-low-density lipoprotein; **HDL:** High-density lipoprotein; **TG:** Triglycerides; FFA: Free fatty acids; **PPD:** p-phenylenediamine; **SOD:** Superoxide dismutase; **CAT:** Catalase; **GPx:** Glutathione peroxidase; **GST:** Glutathione-S-transferase; **GRx:** Glutathione reductase; **CDNB:** 1-chloro-2,4-dinitrobenzene; **TCA:** Trichloroacetic acid; **H & E:** Haematoxylin and Eosin; **EELPM:** Ethanol extract of Phyllanthus maderaspatensis leaves.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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Cite this article: Balraj D, Venkatesh Babu KC, Shabana Begum M. Therapeutic Potential of *Phyllanthus maderaspatensis* Extract on Isoproterenol-Induced Myocardial Infarction: An *in vivo* Examination. Asian J Biol Life Sci. 2026;15(2):419-28.