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Cardioprotective Potential of Mace (Myristica fragrans) Against Isoproterenol-Induced Myocardial Infarction in Rats.

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Abstract

Background: Myocardial Infarction is a major cause of cardiovascular mortality and is associated with oxidative stress and myocardial damage. The present study evaluated the cardioprotective potential of mace from Myristica fragrans against Isoproterenol-induced myocardial infarction in rats.

Methods: Ethanolic extract of mace was administered orally (100, 200, and 300 mg/kg) to Wistar Albino Rats for 15 days. Myocardial infarction was induced using isoproterenol (85 mg/kg, s.c.) on days 14 and 15. Cardioprotective effects were evaluated using ECG changes, heart rate, cardiac biomarkers (CK-MB, LDH, troponin-I), antioxidant parameters (SOD, CAT, MDA), and histopathological analysis.

Results: Isoproterenol significantly increased cardiac biomarkers, lipid peroxidation, ST-segment elevation, and heart rate while reducing antioxidant enzymes. Pretreatment with Myristica fragrans extract significantly reversed these changes in a dose-dependent manner. The 300 mg/kg dose showed the most pronounced protection, restoring biochemical parameters and myocardial architecture near normal levels.

Conclusion: Myristica fragrans exhibits significant cardioprotective activity against isoproterenol-induced myocardial injury, likely due to its antioxidant and membrane-stabilizing properties.

Keywords: Myristica Fragrans, Mace, Cardioprotection, Isoproterenol, Myocardial Infarction, Oxidative Stress, Rats.

Introduction

Infarction of Myocardial

Cardiac infarction or acute myocardial infarction (AMI) (from Latin: Infarctus myocardial, MI) are terms used to describe heart attacks. MI is the result of improper blood flow to a portion of the heart, which damages the heart muscle by depriving it of oxygen. An unstable accumulation of plaques, white blood cells, cholesterol, and fat causes a blockage to form in one of The arteries of the heart that provide the heart's blood. MI is characterized by An irregular heartbeat, anxiety, fatigue, nausea, vomiting, shortness of breath, sweating, and chest pain that spreads to the left arm or left the side of the neck,among other symptoms[12] About 64% of MI patients report having no chest pain., which is known as the "silent killer" of MI.[13]

MI is brought on by several things, like as advanced age, tobacco use, elevated blood pressure, elevated LDL, elevated cholesterol, high fat, diabetes, excessive alcohol use, chronic kidney disease, obesity, lack of physical activity, and drug use, including cocaine and amphetamines.[14,15]

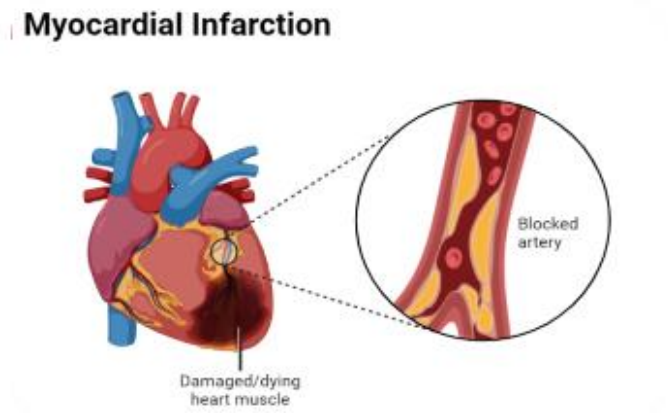


Figure 1: Myocardial injury

Myocardial infarctions can occur "silently," meaning they don't cause any symptoms.[13] These cases may later be found using electrocardiograms, blood enzyme tests, or autopsies after a death. Between 22 and 64 percent of all myocardial infarctions are quiet[14] and are more common in the elderly in those with diabetes mellitus[16] Patients who develop HF after MI and who do so after the first three days after the MI have a 43 percent increased probability of dying . One of the potentially lethal coronary events linked to SCD is myocardial ischemia (MI), The worst possible clinical sign of coronary artery disease (CAD)[17,18], Patients may exhibit pressure or discomfort in the chest that travels to the arm, shoulder, mouth, or neck. Aside from the history and physical examination, myocardial ischemia can also be linked to increased biochemical markers such cardiac troponins and irregularities in the ECG.[19,20]

Pathophysiology of MI

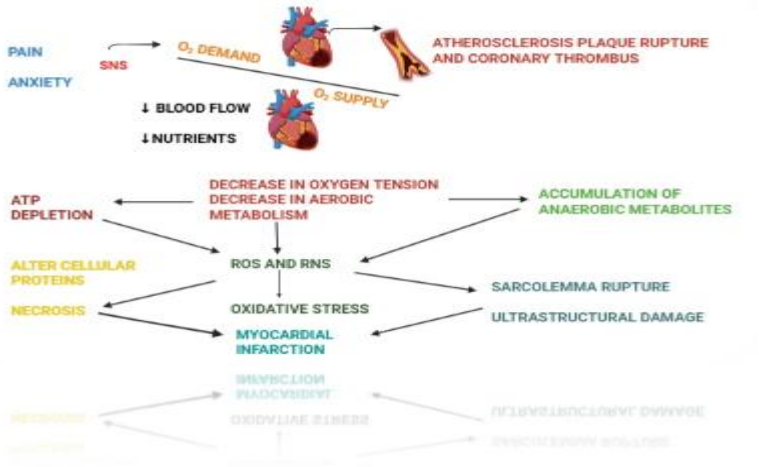


Figure 1: pathophysiology of myocardial infarction

Methodology

Collection of Plant (Mace): Mace collected from loacal market of Jaipur. The sample authenticated in pharmacognocy Department of NIMS Institute of Pharmacy, Jaipur plant ref.(NU/Nip/2025/596). The aril part mace cleaned, dried and powdered; the powder used for the preparation of extract.

In accordance with Thai Herbal Pharmacopoeia guidelines, dried plant materials were assessed for quality standards.

Animals

The Animal were obtained from Animal House at NIMS University Jaipur, Rajasthan, under registration number 1203/PO/Re/S/09/CPCSEA, in compliance with the guidelines set forth by CCSEA, Government of India, New Delhi, India. The Wistar Albino Rats (200-250 gm of either sex) utilized in this investigation. Under the direction of CPCSEA, New Delhi, India. The NIMS University, Institutional Animal Ethics Committee (IAEC-II, 2024) has approved the experimental protocol, Proposal no. NIMSUR/IAEC-02/2024/14.

Preparation of mace extract

Myristica fragrans (mace) were cleaned and dried in an oven set to 45°C for a full day. Dried plant materials were assessed for quality standard following Herbal Pharmacopoeia standards. The extraction of powder was carried out using Soxhlet apparatus with 95% ethanol then evaporator was used for separate out of extract. The extract powder was obtained using water bath. The Myristica fragrans extract yield (8.5%) obtained after extraction.

This yield indicates an effective extraction of bioactive constituents such as phenols, eugenol, flavonoids, and essential oils known to contribute to the antioxidant and cardioprotective effects observed in subsequent experimental evaluations.

Isoproterenol induced myocardial infarction

A standardized dose of ISP 85 mg/kg body weight was injected subcutaneously (s.c.) for two consecutive days, at 24 h interval to induce MI in rats

Experimental Design

Albino Wistar rats either sex (200 gm- 250 gm) randomly divided into five groups, each group consisting six animals. Myocardial infarction induced by subcutaneous (sc) injection of isoproterenol hydrochloride at a dose of 85 mg/kg body weight, dissolved in physiological saline, administered on two consecutive days—the 14th and 15th days of the experiment. The group were divided in following manner-

Table1

Group 1	Control group (normal saline)
Group 2	Isoproterenol (ISO)-induced MI group (85 mg/kg, S.C) for two consecutive days)
Group 3	Isoproterenol (ISO) + Mace (Myristica fragrans) 100 mg/kg
Group 4	Isoproterenol (ISO) + Mace (Myristica fragrans) 200 mg/kg
Group 5	Isoproterenol (ISO) + Mace (Myristica fragrans) 300 mg/kg

Electrocardiography and heart rate.

Needle electrodes were placed and changes in lead II were recorded 12 h after second dose of isoproterenol, on an electro-cardiograph, by using (BPL, CARDIART 108 -DIGI MODEL SINGLE CHANNEL). This heart rate and ECG recording were made in anesthetized animal for 1 mint. Every 5 min. the type of alteration (ST-segment elevation of depression) in normal and experimental animal was considered.

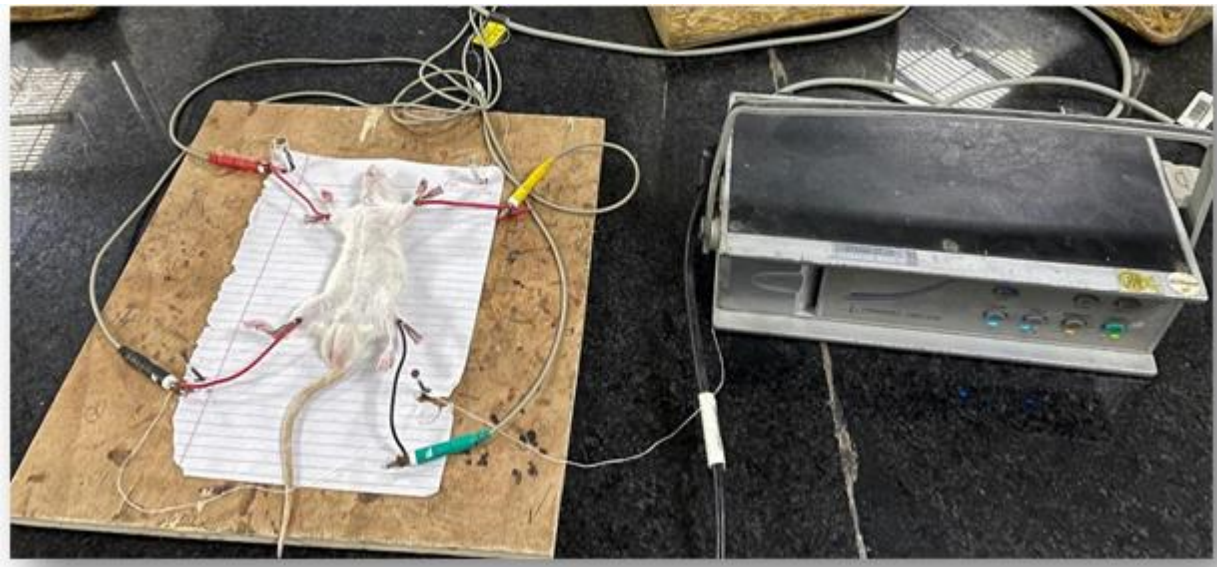


Figure 3: Anesthetized Rat ECG recorded

Surgical Preparations

Each animal's heart rate is recorded using an ECG (BPL CARDIAART 108TDIGI, New Delhi, India) upon dissection, and a blood sample is taken. Following the, blood veins are cut, removing them from their body. And taking out the heart. The heart sends the entire animal sample for testing after store in 10% formalin.

Blood sampling

After experimental period of 15 days, the animals sacrifice and blood withdrawn from the cardiac puncture, following a span of 24h fasting period. The serum separated by centrifugation and used for the biochemical estimation. The blood samples spun at 4^0 C and 2000 rpm for 15 min. blood serum preserved at -20^0C for further study of cardiac biomarkers'

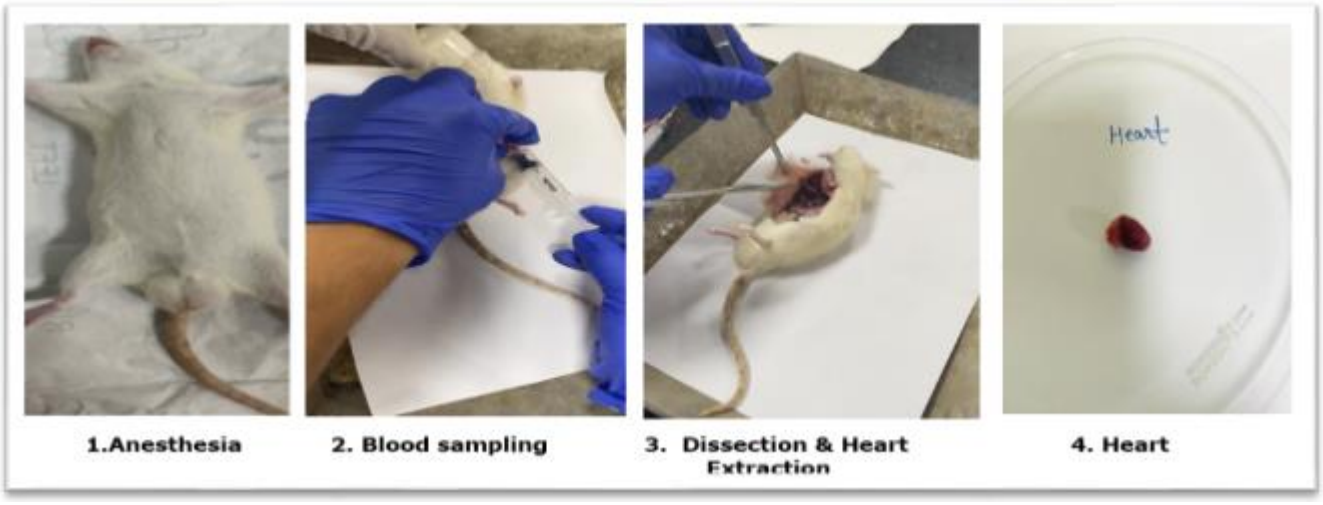


Figure 4: Experimental procedure

Table 2: Experimental Groups

Sn.	Groups	Treatment	No. Of Animals (30)
1	Control	Normal Saline	6
2	Disease Control	Isoproterenol (85mg/kg)	6

3	Treatment Group 1	MFME 100mg/kg	6
4	Treatment Group 1	MFME 100mg/kg	6
5	Treatment Group 1	MFME 100mg/kg	6

Estimation of LDH, CK-MB and Troponin

Lactate Dehydrogenase (LDH) assay: The enzyme lactate dehydrogenase, which is found in practically every bodily tissue, is measured by the LDH Assay, a biochemical test. Using NAD+ as a cofactor, LDH catalyzes the interconversion of lactate to pyruvate. LDH is a nonspecific indicator of tissue damage since it is released into the bloodstream when cells are injured or killed. Utilizing the integrated VITROUS system 5600 apparatus, LDH was determined in coronary fluid.

Principle

Reaction catalysed by LDH:

$$\text{Lactate} + NAD^{+} \xrightarrow{LDH} \text{Pyruvate} + NADH + H^{+}$$

The resulting pyruvate is connected to the appropriate hydrazone by 2,4-DNPH, giving an alkaline medium a brown hue. This color's intensity, which is determined spectrophotometrically at 440 nm, is related to the level of LDH activity.

Creatine - Kinase (CK-MB) Assay

Creatine Kinase (CK) is an enzyme that catalyzes the conversion of creatine + ATP ⇌ creatine phosphate + ADP, providing energy for muscular contraction. CK has 3 isoenzymes: CK-MM (skeletal muscle), CK-BB (brain), CK-MB (heart muscle — Myocardial Band).CK-MB is highly specific to cardiac tissue and is released into the bloodstream when cardiac myocytes are damaged, making it a key marker for myocardial infarction (MI).

Principle:

CK-MB catalyzes the reaction:

$$\text{Creatine Phosphate} + ADP \xrightarrow{CK} \text{Creatine} + ATP$$

The forward process is catalyzed by CPK at pH 7.4. The resultant creatine turns pink when it combines with diacetyl and naphthol in an alkaline media. This color's intensity is spectrophotometrically assessed at 520 nm and is proportional to the enzyme activity. As activators, cysteine and Mg2+ are introduced. The enzyme is rendered inactive by the p-chloromercuric benzoate, which halts the process.

Figure 5: Sample loading and CK-MB, LDH estimation machine (VITROUS 5600)

Estimation of Anti Oxidetavi Stress.

Superoxide Dismutase (SOD)

SOD enzymes, such as SOD1 and SOD2, catalyze the conversion of superoxide radicals into hydrogen peroxide and oxygen. SOD activity is vital for protecting cells from oxidative damage. Alterations in SOD levels have been linked to various diseases, including cardiovascular and neurodegenerative conditions.

Principle:

SOD enzymes catalyze the dismutation of superoxide radicals into molecular oxygen (O_2) and hydrogen peroxide (H_2O_2)

$2O2•−+2H+→O2+H2O22\ O_2•^-$

In the assay, superoxide radicals are typically generated enzymatically, and their concentration is measured by their ability to reduce a tetrazolium salt, such as WST-1, to a colored formazan product. SOD activity is quantified by the inhibition of this color formation, as SOD enzymes scavenge the superoxide radicals, reducing the rate of formazan production

Catalase (CAT)

An enzyme called catalase prevents oxidative damage by breaking down hydrogen peroxide into oxygen and water. Numerous disorders have been found to have decreased catalase activity, underscoring its function in cellular defense mechanisms.

Principle

The enzyme catalase is present in almost every living thing that comes into contact with oxygen, including bacteria, plants, and animals. It facilitates the breakdown of hydrogen peroxide into oxygen and water.

$2\ H2O2→2\ H2O+O2$

This reaction is vital as hydrogen peroxide is a reactive oxygen species (ROS) that can cause cellular damage. By breaking down H_2O_2, catalase helps mitigate oxidative stress and protects cells from potential harm.

Malondialdehyde (MDA) The **Malondialdehyde (MDA) test** is a widely used method for assessing Lipid peroxidation is the process by which polyunsaturated fatty acids in cell membranes are attacked by reactive oxygen species (ROS)., leading to cellular damage. MDA, a three-carbon aldehyde, is a primary end product of this degradation and serves as an indicator of oxidative damage

Principle

The MDA test usually referred to as the Thiobarbituric Acid Reactive Substances (TBARS) assay, is predicated on the reaction that occurs between MDA and TBA in an acidic, high-temperature environment. This reaction forms a red-colored MDA-TBA_2 adduct, which can be quantified spectrophotometrically due to its strong absorbance at **532 nm.**

Histopathological Examination:

Animals were sacrificed at the conclusion of the trial., and hearts were carefully excised, washed with cold saline, and fixed in 10% formalin for 24–48 hours. The fixed tissues were processed by dehydration in graded alcohol series, cleared in hematoxylin and eosin (H&E) staining to. Sections of 4–5 µm thickness were cut using a microtome and mounted on glass slides. These sections were stained with hematoxylin and eosin (H&E) to observe general histoarchitecture. The stained slides were examined under a light microscope to assess myocardial integrity, necrosis, inflammatory infiltration, and vascular changes, indicating the extent of cardioprotection or injury. Heart tissues

examined for histological changes using hematoxylin and eosin (H&E) staining to assess the extent of myocardial damage and inflammation.

Statistical Evaluation

The data were tabulated and computed using Excel workbooks. Every statistical investigation was carried out using the relevant statistical software. The areas at risk measurements the student t test was used to compare them, and the groups with different Body weights, heart weights and infarct sizes were analyzed using different changes in the study. A cardiac echo was also performed. The data is displayed as Mean ± SEM.

Results and Discussion

MFME exhibited a dose-dependent trend in modulating cardiac hypertrophy, with the 100 mg/kg dose showing the most prominent protective effect against isoproterenol-induced cardiac enlargement.

Table 3: Comparison of body weight, heart weight ratio in experimental groups

Sn.	Groups	Heart weight(g)	Body weight(g)	HW/BW($x10^{-3}$)
1	Control	0.53±0.07	237.83±10.32	0.22±0.03
2	Isoproterenol 85mg/kg	0.57±0.04	238.50±9.98	0.24±0.02
3	MFME 100mg/kg	0.48±0.04	241.67±4.50	0.20±0.02
4	MFME 200mg/kg	0.55±0.09	242.33±5.82	0.23±0.04*
5	MFME 300mg/kg	0.63±0.06	240.67±6.39	0.26±0.03*

Data are expressed as Mean ± SEM (n=6 for each group) *p<0.005 as compared to normal control, P<0.005 compared to control analyzed one-way ANOVA A followed by Tukey Kramer's multiple comparison test.

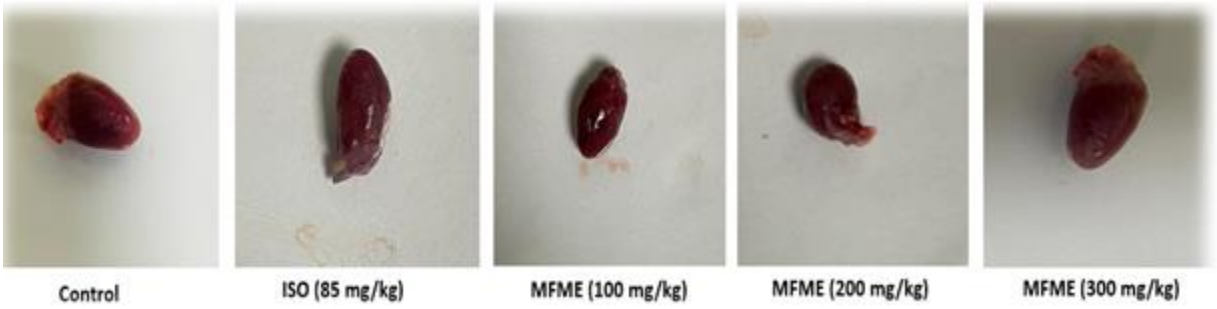


Figure 6: Various groups heart image

Heart rate

Each experimental group's average heart rate (HEART BEAT) and standard deviation are shown in the table

Treatment with Myristica fragrans extract led to a dose-dependent reduction in heart rate:

- At 100 mg/kg, HR was 385.00 ± 16.25 beats/min
- At 200 mg/kg, HR dropped to 357.50 ± 3.58 beats/min
- At 300 mg/kg, HR further declined to 336.33 ± 8.16 beats/min, approaching normal levels and showing highly significant protection

These findings indicate that Myristica fragrans extract effectively attenuates isoproterenol-induced tachycardia, particularly at higher doses, helping restore cardiac rhythm toward baseline.

Table 4: heart beats (beats/min)

Sn.	Groups	HR (beats/min)	ST elevation (mV)
1	Control	317.83±19.55	0.197±0.019[a]
2	Isoproterenol 85mg/kg	428.33±24.09[a]	0.343±0.027[b]
3	MFME 100mg/kg	385±16.25	0.288±0.023*
4	MFME 200mg/kg	357.50±3.58	0.24±0.02**
5	MFME 300mg/kg	336.33±8.16	0.222±0.019**

values are expressed as mean SEM. N=5, all data were subjected to one-way ANOVA followed by Dunnett's test [a]p<0.05 against control group b p<0.05 against isoproterenol group.

ST segment Elevation Analysis

ST segment elevation was analyzed as an electrocardiographic marker of myocardial injury. The normal (control) group exhibited a baseline ST elevation of 0.197 ± 0.019 mV, indicating normal cardiac electrical activity. In contrast, the isoproterenol-treated (ISO) group showed a significant increase in ST segment elevation to 0.343 ± 0.027 mV ($p < 0.001$ vs. control), confirming myocardial ischemia and damage.

Treatment with Myristica fragrans extract resulted in a dose-dependent reduction in ST elevation:

- The Mace 100 mg/kg showed an ST elevation of 0.288 ± 0.023 mV ($p < 0.01$ vs. toxic),
- The Mace 200 mg/kg showed a further reduction to 0.240 ± 0.020 mV ($p < 0.001$),
- The Mace 300 mg/kg exhibited an ST elevation of 0.222 ± 0.019 mV, which was very close to normal values and also highly significant ($p < 0.001$ vs. toxic).

These results suggest that Myristica fragrans extract significantly attenuates isoproterenol-induced ST segment elevation in a dose-dependent manner, indicating its strong cardioprotective effect by restoring normal electrical conduction and reducing myocardial ischemia.

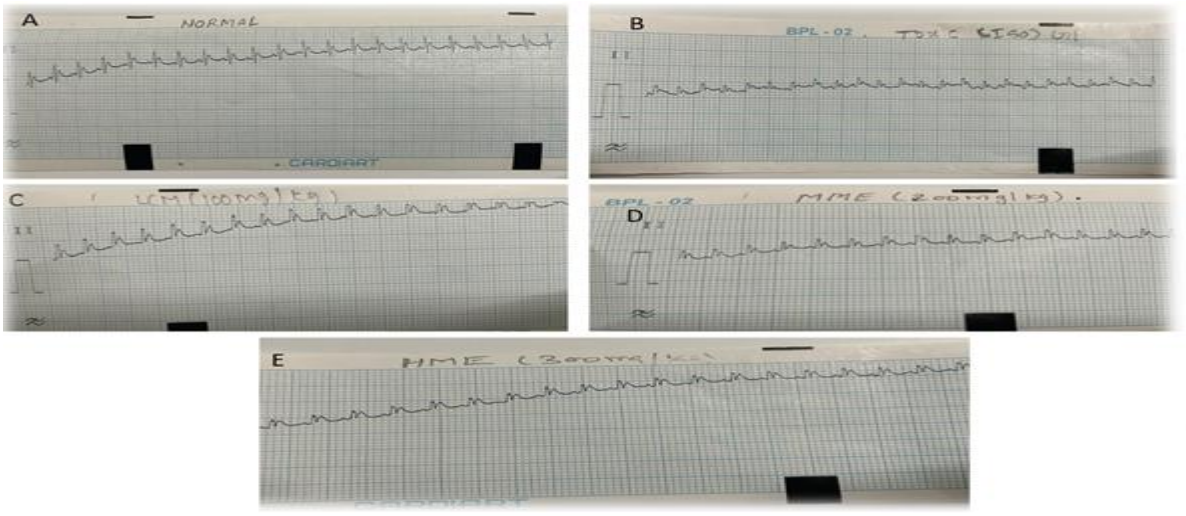


Figure 7: Effect of pretreatment with MFME (100,200 and 300 mg)for 15 days in ISO-induced myocardial infarcted animal action (ST-elevation, electrocardiogram (ECG).

Cardiac Biomarker

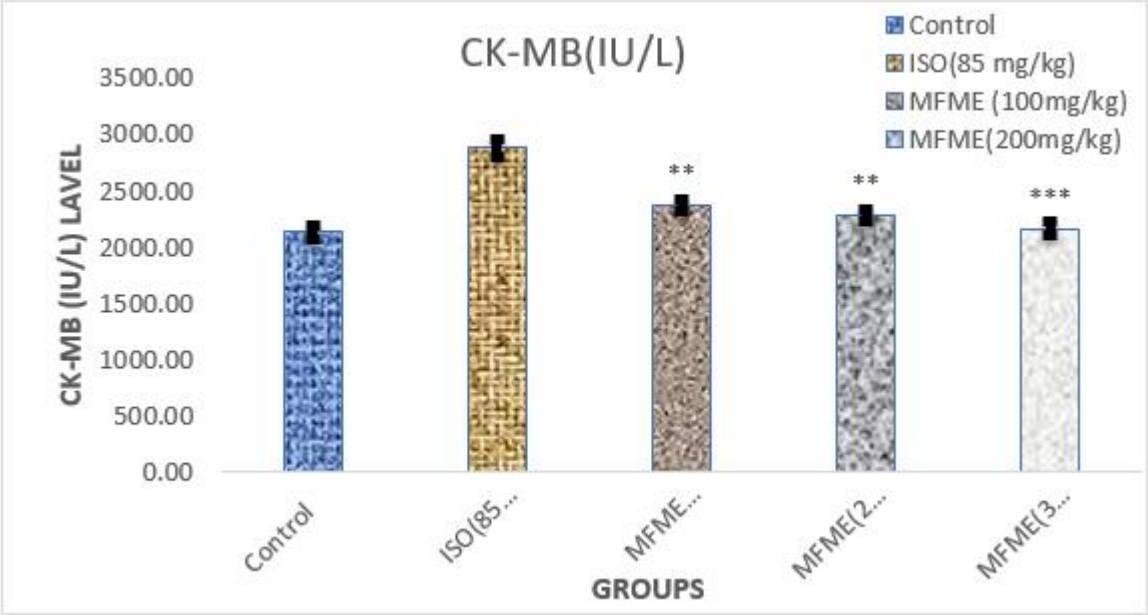
Creatine-Kinase myoglobin (CK-MB) Estimation:

These results show that Myristica fragrans (Mace) has potential cardioprotective qualities and can efficiently and dose-dependently reduce the myocardial damage caused by isoproterenol. The plant's therapeutic promise in treating cardiac damage is supported by the decrease in CK-MB levels, especially at larger dosages.

Table 5: Effect of Myristica fragrans on CK-MB Levels in ISO-Induced Myocardial Injury

Sn.	Groups	Creatine Kinase MB level (U/L)
1	Control	2127.50±63.37
2	Isoproterenol 85mg/kg	2879.83±77.20***[a]
3	MFME 100mg/kg	2363.5±54.40** [b]
4	MFME 200mg/kg	2279.66±49.99** [b]
5	MFME200mg/kg	2155.66±62.18*** [b]

values are expressed as mean SEM. N=6, all data were subjected to one-way ANOVA followed by tukey test. [a]p<0.001 against control group, b (p<0.01), [b]p<0.001 against isoproterenol group



Graph 1: Values are expressed as mean SEM. N=6, all data were subjected to one-way ANOVA followed by tukey test. [a]p<0.001 against control group, b (p<0.01), [b]p<0.001 against isoproterenol group.

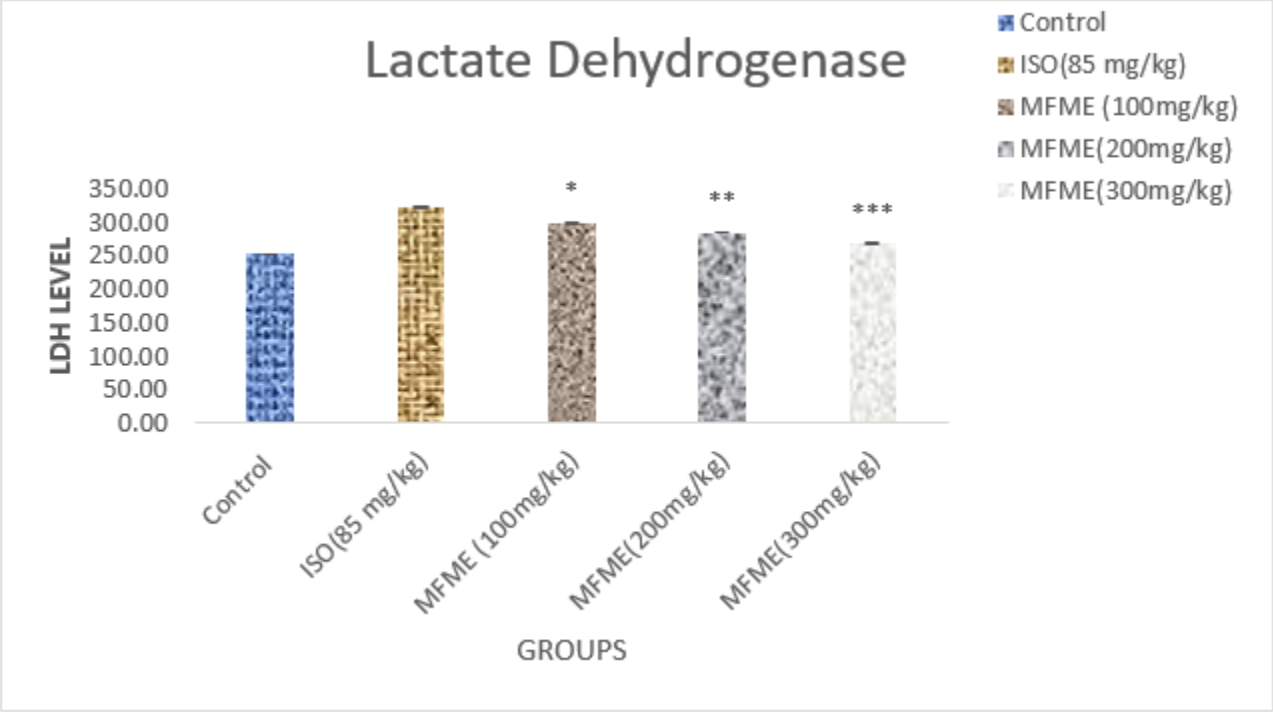
Lactate Dehydrogenase (LDH) Level Analysis

The ability of Myristica fragrans to preserve cellular integrity and stop enzymatic leakage under cardiac stress may be the reason for these observations, which collectively support the plant's cardioprotective potential. The results are expressed as mean ± standard error of the mean (SEM). . a (p< 0.05) was considered statistically significant.

Table 6: Effect of Myristica fragrans on LDH Levels in ISO-Induced Myocardial Injury

Groups	Lactate Dehydrogenase (U/L)
Control	251.33±21.87
Isoproterenol (85 mg/kg)	321.83±6.96 ***[a]
MFME 100mg/kg +ISO (85 mg/kg)	297.17±12.2 *[b]
MFME 200mg/kg +ISO (85 mg/kg)	283.67±13.68 **[b]
MFME200mg/kg +ISO (85 mg/kg)	266.67±15.72 *** [b]

The data are presented as mean ± standard error of mean (SEM). Statistical significance was assessed using one-way ANOVA followed by Tukey's post hoc test, with *p < 0.05, **p < 0.01, ***p < 0.001 considered significant



Graph 2: The data are presented as mean ± standard error of mean (SEM). Statistical significance was assessed using one-way ANOVA followed by Tukey's post hoc test, with a*p < 0.05, **p < 0.01, ***p < 0.001 considered significant.

Troponin-I – Marker of Cardiac Injury

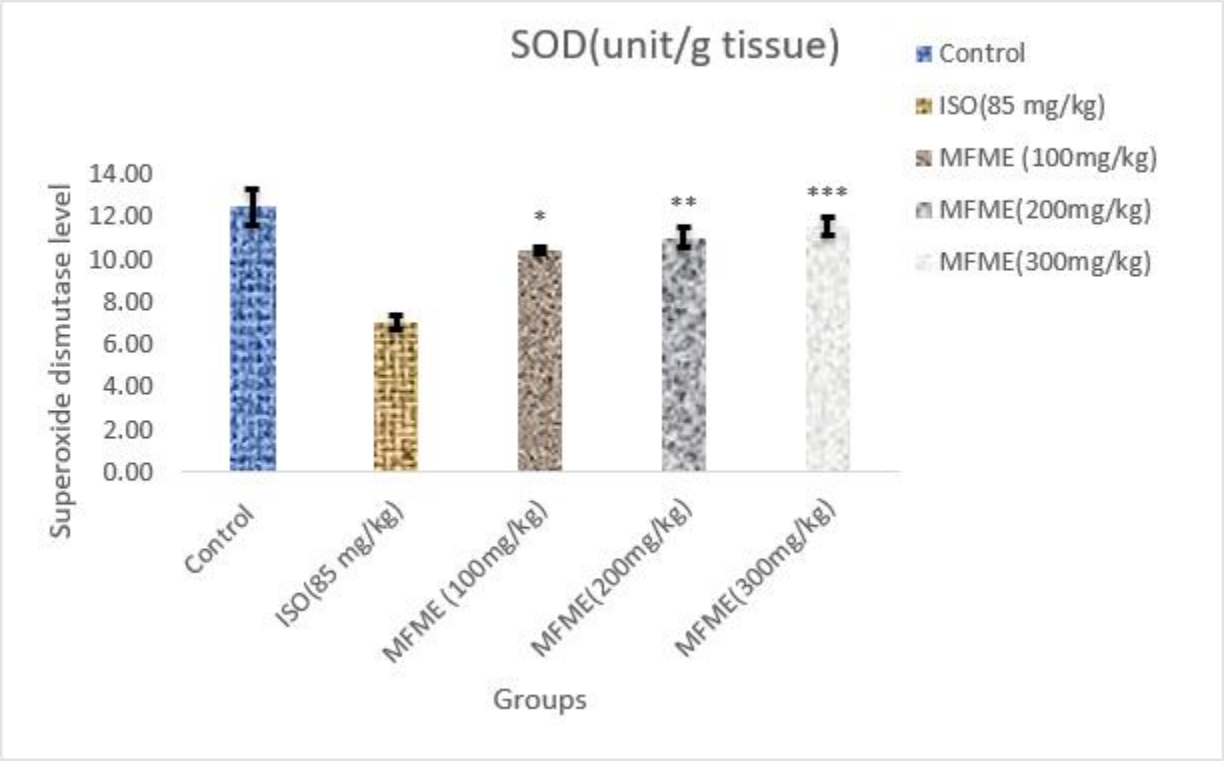
The control group showed minimal levels of troponin-I, while the isoproterenol (ISO)-treated group exhibited a significant elevation, indicating substantial myocardial injury. Pretreatment with mace extract at doses of 100, 200, and 300 mg/kg led to a dose-dependent reduction in serum troponin-I levels.

Table 7: Effect of Myristica fragrans on Troponin-I Levels in ISO-Induced Myocardial Injury

Sn.	Groups	Troponin-I(pg./ml)
1	Control	0.75±0.14
2	Isoproterenol (85 mg/kg)	2.64±0.17 ***[a]
3	MFME 100mg/kg +ISO (85 mg/kg)	2.38±0.19* [b]

4	MFME 200mg/kg +ISO (85 mg/kg)	1.74±0.14** [b]
5	MFME200mg/kg +ISO (85 mg/kg)	1.26±0.12*** [b]

The data are presented as mean ± standard error of mean (SEM). Statistical significance was assessed using one-way ANOVA followed by Tukey's post hoc test, with *p < 0.05, **p < 0.01, ***p < 0.001 considered significant.



Graph 3: The data are presented as mean ± standard error of mean (SEM). Statistical significance was assessed using one-way ANOVA followed by Tukey's post hoc test, with *p < 0.05, **p < 0.01, ***p < 0.001 considered significant.

MDA – Lipid Peroxidation Marker

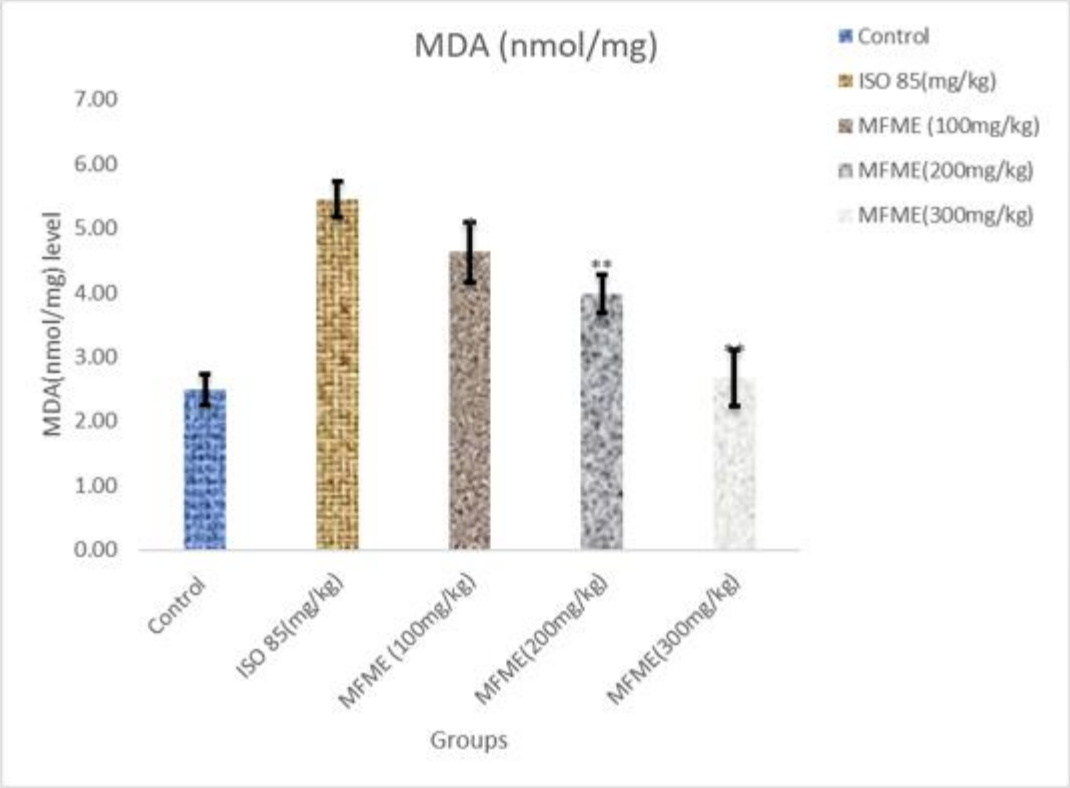
Malondialdehyde (MDA) levels, a marker of oxidative stress and lipid peroxidation, are displayed for each treatment group in the data. The mean MDA level in the control group was 2.49 ± 0.24. On the other hand, oxidative myocardial damage was shown by the considerable increase in MDA to 5.44 ± 0.28 in the group treated with isoproterenol (85 mg/kg). MDA levels decreased in a dose-dependent manner after receiving treatment with Myristica fragrans. MDA dropped to 4.63 ± 0.47 at 100 mg/kg and then to 3.97 ± 0.30 at 200 mg/kg. The MDA level was remarkably reduced to 2.67 ± 0.43 at 300 mg/kg, which is close to near-control values. These results imply that Myristica fragrans has strong cardioprotective and antioxidant qualities, which enable it to reduce isoproterenol-induced oxidative stress in a dose-dependent way.

Table 8: Effect of Myristica fragrans on MDA Levels (nmol/mg protein)

Sn.	Groups	MDA (nmol/mg protein)
1	Control	2.49±0.24
2	Isoproterenol (85 mg/kg)	5.44±0.28***[a]

3	MFME 100mg/kg +ISO (85 mg/kg)	4.63±0.47* [b]
4	MFME 200mg/kg +ISO (85 mg/kg)	3.97±0.30** [b]
5	MFME 300mg/kg +ISO (85 mg/kg)	2.67±0.43*** [b]

The data are presented as mean ± standard error of mean (SEM). Statistical significance was assessed using one-way ANOVA followed by Tukey's post hoc test, with *p < 0.05, **p < 0.01, ***p < 0.001 considered significant.



Graph 4: The data are presented as mean ± standard error of mean (SEM). Statistical significance was assessed using one-way ANOVA followed by Tukey's post hoc test, with *p < 0.05, **p < 0.01, ***p < 0.001 considered significant .

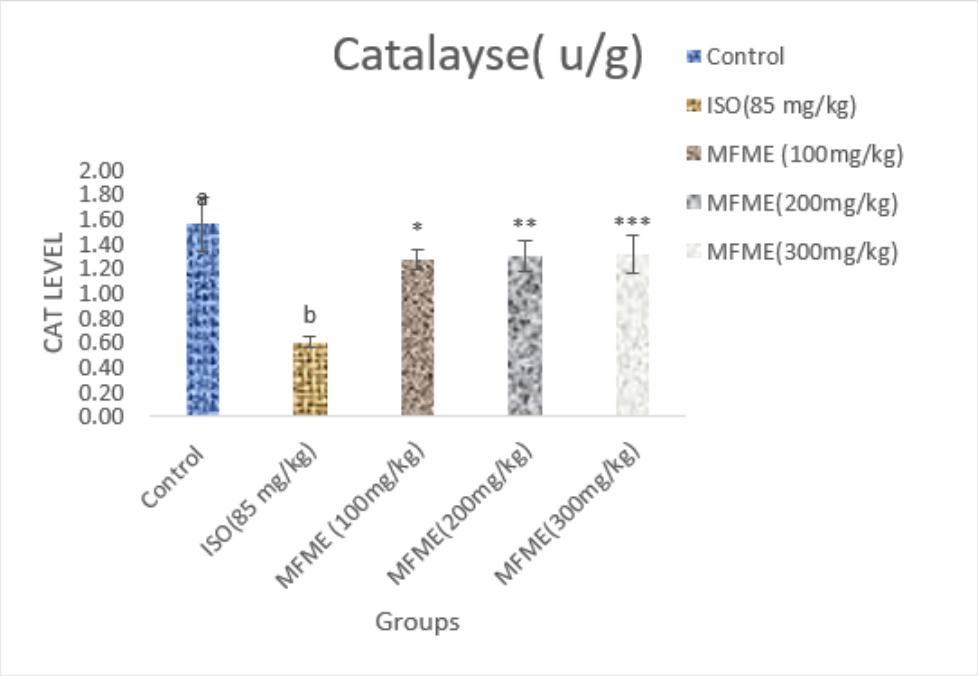
Catalase

As Myristica fragrans dosages increase, catalase activity gradually improves, indicating a strong antioxidative action. By increasing endogenous catalase activity, the extract seems to prevent oxidative damage and lessen the buildup of reactive oxygen species.

Table 9: Effect of Myristica fragrans on catalyzes enzyme (u/g)

Sn.	Groups	CAT(u/g)
1	Control	1.56±0.23
2	Isoproterenol (85 mg/kg)	0.60±0.05***[a]
3	MFME 100mg/kg +ISO (85 mg/kg)	1.28±0.08** [b]
4	MFME 200mg/kg +ISO (85 mg/kg)	1.30±0.13** [b]
5	MFME 300mg/kg +ISO (85 mg/kg)	1.32±0.16*** [b]

The data are presented as mean ± standard error of mean (SEM). Statistical significance was assessed using one-way ANOVA followed by Tukey's post hoc test, with a*p < 0.05,b **p < 0.01, b ***p < 0.001 considered significant this groups are compared to against A toxic groups.



Graph 5: The data are presented as mean ± standard error of mean (SEM). Statistical significance was assessed using one-way ANOVA followed by Tukey's post hoc test, with *p < 0.05, **p < 0.01, ***p < 0.001 considered significant .

Histopathological Result

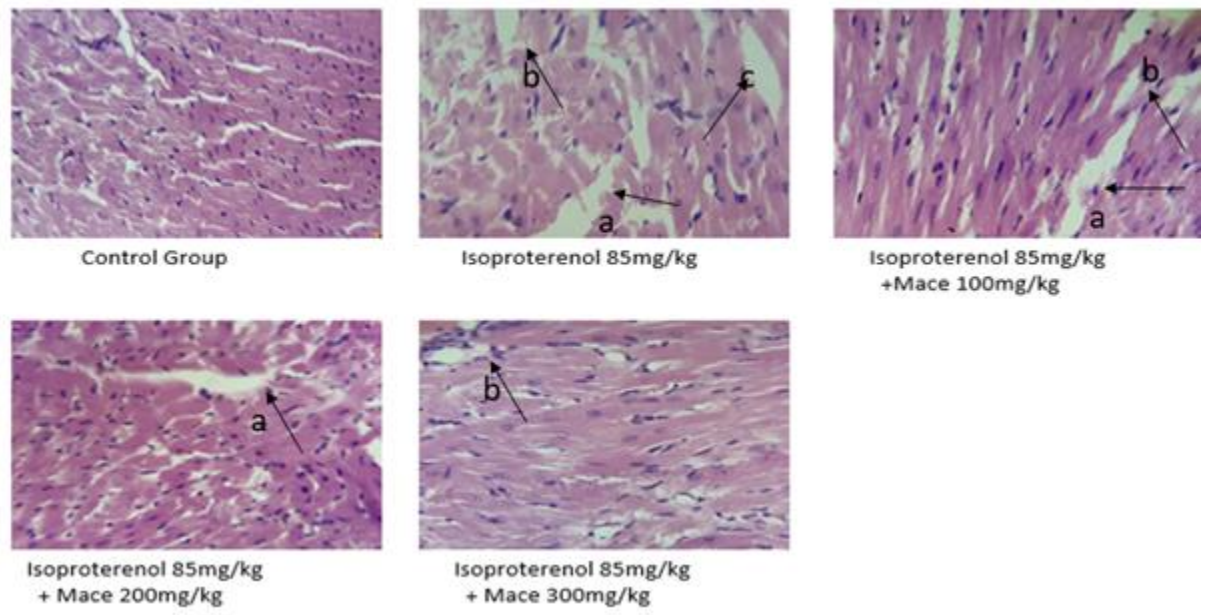


Figure 8: Histopathological image of heart section after Hematoxylin and Eosin staining (400x), (A =Oedema. B Necrosis C=Inflammatory infiltration.)

Table 10: Hestoptathological Experimental Groups

Sn.	Groups	Oedema	Necrosis	Inflammatory Infiltration
1	Control	____	_____	____
2	Isoproterenol (85 mg/kg)	+++	+++	+++
3	MFME 100mg/kg +ISO (85 mg/kg)	++	++	++
4	MFME 200mg/kg +ISO (85 mg/kg)	+	++	++
5	MFME 300mg/kg +ISO (85 mg/kg)	+	+	+

- Isoproterenol caused severe oedema, infiltration, and necrosis (mean scores ~3).
- All Mace-treated groups showed statistically significant improvements (reduced scores).
- 200 mg/kg and 300 mg/kg doses showed highly significant protection ($p < 0.001$) across all parameters.
- 300 mg/kg dose was most effective, nearly restoring histological integrity to control levels.

Conclusion

The present study demonstrates the potent cardioprotective effect of Myristica fragrans (mace) Ethanolic extract (MFME) against isoproterenol (ISO)-induced myocardial infarction in rats. ISO administration caused significant cardiac damage, as evidenced by elevated serum markers (CK-MB, LDH, and troponin), increased lipid peroxidation (MDA), diminished antioxidant enzyme activity (SOD and catalase), ECG abnormalities (ST-segment elevation, altered R-wave amplitude), and histopathological alterations including oedema, necrosis, and inflammatory infiltration. These results reaffirm that oxidative stress plays a central role in ISO-induced cardiac injury. Treatment with MFME markedly attenuated these pathological changes in a dose-dependent manner. Among the tested doses, 300 mg/kg offered the most pronounced protection, restoring biochemical parameters close to normal, reducing myocardial oxidative burden, preserving cellular antioxidant defense, and improving ECG and histological architecture of cardiac tissue. The cardioprotective effects are likely attributed to the rich phytoconstituents in mace, which possess strong free radical scavenging, membrane-stabilizing, and anti-inflammatory properties. The extract's ability to restore antioxidant enzyme levels and reduce lipid peroxidation further supports its role in mitigating myocardial injury. Overall, the findings suggest that Myristica fragrans exerts significant protective effects against ISO-induced myocardial infarction by combating oxidative stress and preserving myocardial integrity. These results support the traditional use of mace in cardiovascular health and encourage further studies to isolate active constituents and elucidate underlying molecular mechanisms. With proper standardization and clinical validation, M. fragrans may of a promising natural cardioprotective agent for therapeutic use.

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