

# Emphasizing the Cardioprotective Efficacy of *Basella alba* in an *In vivo* Model of Isoproterenol-Induced Cardiac Injury

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Received August 18, 2024; Revised October 24, 2025; Accepted December 31, 2025

## Cite This Paper in the Following Citation Styles

(a): [1] Jyothi Basini, Sreenivasulu P, Niranjana Babu M, Dharma Swathi, Sorta Ganesh, "Emphasizing the Cardioprotective Efficacy of *Basella alba* in an *In vivo* Model of Isoproterenol-Induced Cardiac Injury," *Advances in Pharmacology and Pharmacy*, Vol. 14, No. 1, pp. 1 - 11, 2026. DOI: 10.13189/app.2026.140101.

(b): Jyothi Basini, Sreenivasulu P, Niranjana Babu M, Dharma Swathi, Sorta Ganesh (2026). *Emphasizing the Cardioprotective Efficacy of Basella alba in an In vivo Model of Isoproterenol-Induced Cardiac Injury*. *Advances in Pharmacology and Pharmacy*, 14(1), 1- 11. DOI: 10.13189/app.2026.140101.

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**Abstract Purpose of the Study:** This study provides valuable insights into the cardioprotective effects of *Basella alba* in a rat model of isoproterenol-induced myocardial infarction (MI). The focus of the research was to explore how the methanolic extract of *Basella alba* (MEBA) can influence myocardial injury markers, oxidative stress, and inflammation, offering a potential natural therapeutic approach for MI. **Materials and Methods:** The study uses a rat model where thirty male *Wistar* rats are divided into five groups. These groups include a control group, an MI-induced group with isoproterenol, and treatment groups receiving atenolol and two different doses of MEBA 100 mg/kg and 200 mg/kg, p.o. The animals are treated for 30 days before being administered isoproterenol, which is known to induce myocardial infarction by disrupting coronary blood flow and causing cardiac tissue damage. **Results:** Markers of myocardial injury such as LDH, CPK, AST, and ALT, were significantly reduced ( $p < 0.001$ ) in the extract-treated groups, compared with the negative control group, suggesting that MEBA can effectively mitigate myocardial damage following an ischemic event. The antioxidant enzyme activities like SOD, MDA and CAT were enhanced significantly ( $p < 0.001$ ) in the treated groups, while lipid peroxidation was reduced significantly ( $p < 0.001$ ) when compared to the negative control in both

serum and heart tissue homogenate samples. Histological analysis revealed reduced myocardial damage in the groups treated with *Basella alba*, especially in comparison to the untreated MI group, where significant tissue damage and necrosis were observed. This underscores the potential tissue-protective effects of the extract. **Conclusion:** The study suggests that the methanolic extract of *Basella alba* has significant cardioprotective properties, reducing both myocardial injury and oxidative stress markers in an isoproterenol-induced MI rat model.

**Keywords** Myocardial Infarction, Oxidative Stress, Isoproterenol, *Basella alba*, Cardiac Biomarkers

## 1. Introduction

The acute myocardial infarction (AMI) model in rats is frequently used to replicate human cardiovascular disease, specifically to study cardiac signalling mechanisms related to heart failure (HF) and to evaluate therapeutic strategies for HF management [1]. Myocardial infarction (MI) disrupts the heart's mechanical, electrical, structural, and biochemical properties, leading to compromised cardiac function and significant morbidity and mortality

across both developing countries, like India, and developed countries, such as the U.S. [2]. MI is often accompanied by biochemical changes, including hyperlipidaemia, lipid peroxidation (LPO), and free radical damage, which result in alterations to the myocardium. The complications from MI make it a leading cause of death for both men and women [3].

In developing countries, particularly in all areas with changing lifestyles, MI is increasingly contributing to mortality rates. Plants enriched with antioxidant compounds have demonstrated protective effects against various diseases, maintaining their therapeutic efficacy [4]. There is a growing interest in using natural antioxidants as a protective measure against cardiovascular issues, such as ischemia-reperfusion injury [5]. Isoproterenol, a synthetic catecholamine and  $\beta$ -adrenergic agonist, induces severe myocardial stress and infarct-like necrosis in heart muscles. It disrupts myocardial membrane permeability, leading to functional loss and damage to myocardial membranes. Isoproterenol-induced myocardial necrosis is a standard model for studying the benefits of various drugs on cardiac dysfunction. Although modern drugs can prevent cardiovascular disorders, their use is often limited by side effects [6-9].

Many plant-based products are widely used for their health benefits. *Basella alba*, a rapidly growing and heat-tolerant perennial vine from the Basellaceae family, is known by various names, including Malabar spinach, Indian spinach, Ceylon spinach, and Chinese spinach. Although it is rare in its natural habitat, it is increasingly cultivated for its nutritional value in temperate and tropical regions [10]. Traditionally, in Ayurveda medicine, the leaves of *Basella alba* are used to promote restful sleep when applied to the head before bathing. Additionally, the plant has demonstrated anti-inflammatory, antioxidant, anti-diabetic, and central nervous system depressant activities [11]. Given its traditional significance and these reported activities, this study investigates the cardioprotective effects of the methanolic extract of *Basella alba* leaves in an isoproterenol-induced myocardial infarction model in male Wistar rats.

## 2. Materials and Methods

### 2.1. Experimental Animals

Male Wistar rats numbering 30 of 8 weeks old, weighing 160–210 g, were obtained from the laboratory animal centre and were housed in solid bottom polycarbonate cages under controlled environmental conditions ( $22 \pm 3^\circ\text{C}$  with 30 - 70% humidity and a 12/12-hour light/dark cycle). The rats were acclimatized to the environment for 1 week prior to the initiation of the experiment. The rats were purchased from Kedhar bio labs, Mahabubnagar,

Telangana, India. The study has been approved by the Institutional Animal Ethics Committee [IAEC] of the test facility under the project title “Cardioprotective activity of *Basella alba* against isoproterenol induced myocardial infarction with IAEC number TAB/IAEC/AOT/01/24”.

### 2.2. Plants Materials

*Basella alba* is an herb that grows throughout madanapalli in the fields. The plant was collected and was taxonomically identified by the Department of botany, SV University, Tirupathi, India. The leaves were washed and air dried under shade preventing direct sunlight. *Basella alba* leaves were washed in tap water and dried at room temperature for 8 weeks after which they were ground into fine powder. The methanolic extract was prepared by soaking 431 g of the plant powder in 2.65 litres of 70% methanol for 72 h. The mixture was sieved using a cheese cloth after which it was filtered through filter paper. The filtrate was then concentrated by evaporation using a rotary evaporator to obtain a solid mass. The resulting mass of the paste-like extract was 26.5 g with a percentage yield of 6.15%. The solid extract was then re-dissolved in normal saline and stored in capped bottles in a refrigerator at  $4^\circ\text{C}$  until required.

### 2.3. Acute Toxicity Studies

The dose limits were selected on the basis of oral acute toxicity studies in rats, in accordance with the Organization for Economic Co-operation and Development (OECD) guidelines [13]. The acute toxicity test was carried out in 5 rats by giving doses of 5, 50, 300, 2000 mg/kg body weight. All groups of test drug showed neither any toxic effect, nor any lethal effect in the dose range of 2000 mg/kg body weight. So, a minimum dose of 100 mg/kg and 200 mg/kg of body weight was taken for further studies.

### 2.4. Extract Administration

The rats were weighed prior to the administration of the methanolic extract of *Basella alba* to determine the amount to be administered by using a weighing scale. *Basella alba* leaf extract was administered via oral route with the aid of oro-pharyngeal cannula at a low dose of 100 mg/kg and a high dose of 200 mg/kg. During administration, the rats were handled carefully to restrict movement and prevent trauma to them.

### 2.5. Experimental Design

The experimental rats were divided into 5 groups, each consisting of 6 animals.

Group I, the control group, animals in this group received an injection of distilled water (2.5 ml/kg). Group II, the Isoproterenol (ISP) induced myocardial infarction

group, received an injection of ISP, 85 mg/kg of body weight on last 2 days of treatment schedule. Group III, (Standard control) was treated with the drug atenolol (10 mg/kg body weight, *s.c.*) once daily up to 30 days, followed by ISP administration on last 2 days. Group IV, (low dose) the rats were administered with methanolic extract of *Basella alba* (MEBA) 100 mg/kg bw, given orally once daily up to 30 days, followed by ISP administration on last 2 days. Group V, (high dose) the rats were administered with methanolic extract of *Basella alba* (MEBA) at 200 mg/kg bw, given orally once daily up to 30 days, followed by ISP administration on last 2 days. The duration of the treatment was 30 days. At the end of the treatment, blood was collected from all the groups by puncturing the retro-orbital plexus and was allowed to clot at room temperature and serum was separated by centrifugation at 2500 rpm for 10 min. The animals were sacrificed to remove the heart for histopathological studies which would help in assessing the cardiac damage and the protective role of MEBA.

## 2.6. Biochemical Estimation from Serum

The serum was analysed for the presence of different enzymes related to myocardial infarction such as Lactate dehydrogenase (LDH), Creatine kinase-MB fraction (CK-MB), Aspartate transaminase (AST), Alanine transaminase (ALT), Total cholesterol, Total triglycerides (TGL), High density lipoproteins (HDL) and Low-density lipoproteins (LDL) [12-16]. All analyses were performed with commercially available kits based on the references using an analyzer.

## 2.7. Biochemical Estimation from Tissue Homogenate

After sacrificing the rats by cervical dislocation, the heart tissue was excised immediately and washed with chilled isotonic saline. The heart tissue homogenate was prepared in 0.05 M phosphate buffer, pH 7.4 and homogenated in tissue homogenizer at 2,000 rpm for 10 min and used for analyzing antioxidant activities like Lipid peroxides (LPO), Superoxide dismutase (SOD) and Catalase (CAT) activity [17, 18].

## 2.8. Histopathological Studies

After sacrificing the rats by cervical dislocation, some portion of atria and ventricles was collected, washed in normal saline, perfused with 10% formalin and stored in the same for histopathological studies. It was fixed by using 40% formaldehyde as a fixative for 24 hours and dehydrated with alcohol. All tissues were cleaned and embedded by using xylene and molten paraffin wax (melting point 58-60°C). Sections were cut at 5  $\mu$ m thickness and were stained by double staining. To differentiate the nucleus and cytoplasm, the basic dye haematoxylin and the acid dye eosin were used. Electron

micrographs were performed using a transmission electron microscope and photographed by photomicrography. The sections were then viewed under the Nikon microscope, ECLIPSE E400, model 115, Japan [19].

## 2.9. Statistical Analysis

The data were collected, calculated and tabulated as Mean  $\pm$  SD and significant differences between the groups were analyzed by Student's 't' test using SPSS software version 20 and the 'P' values were used to judge the significant level.

## 3. Results

The results of cardioprotective activities of methanolic extract of *Basella alba* against isoproterenol-induced myocardial infarction on serum biochemical parameters, heart tissue homogenate and histopathological studies are presented.

From Table 1, the levels of CPK were found to be 46.19 in Group I normal rats which increased to 156.08 when the rats were treated with ISP. Then the rats on treatment continuously with the plant extract -MEBA (100 mg/kg and 200 mg/kg) for 30 days, showed a decrease in the values, which were found to be 43.36 and 49.15 respectively, which were comparable with the standard drug ISP treated group whose values were found to be 49.03. The levels of LDH were found to be 127.49 in Group I normal rats which increased to 247.52 when the rats were treated with ISP. Then the rats on continuous treatment with the plant extract-MEBA (100 mg and 200 mg) for 30 days, showed a decrease in the values, which were found to be 133.06 and 136.79 respectively, and were comparable with the ISP treated group whose values were found to be 136.22.

But the levels of CPK and LDH reduced in the heart tissue homogenate, when the rats were induced with ISP. But on treatment with the plant extract - MEBA, the levels of CPK and LDH increased because of the cardioprotective activity of the plant which was comparable with the standard drug (atenolol) treatment (Table 2).

The levels of AST and ALT were found to be  $96.40 \pm 1.38$  and  $64.58 \pm 0.88$  in Group I normal rats which increased to  $210.40 \pm 1.21$  and  $173.20 \pm 0.62$  when the rats were treated with ISP respectively (Table 3). Thus, the rats on treatment for 30 days continuously with the plant extract -MEBA showed a decrease in the values, which is comparable with the standard drug atenolol treated group whose values were found to be  $99.16 \pm 0.66$  and  $66.76 \pm 0.60$  for Group III;  $93.35 \pm 1.57$  and  $67.51 \pm 1.28$  for Group IV; and  $99.15 \pm 0.63$  and  $65.93 \pm 1.05$  for Group V. The prevention of the leakage of AST and ALT from the heart tissues in Group IV and Group V suggested a potential protective effect of the plant extract against ISP induced heart damage.

**Table 1.** Effect of methanolic extract of *Basella alba* against ISP induced MI on serum levels of CPK and LDH

S.No	Groups	Treatment Schedule	CPK(IU/L)	LDH(IU/L)
1	Group I (Normal Control)	Distilled water (2.5 ml/kg)	46.19±3.21	127.49±1.17
2	Group II (Negative Control)	Isoproterenol (ISP) <i>s.c</i> 85mg/kg on last 2 days	156.08±3.99 <sup>#</sup>	247.52±1.28 <sup>#</sup>
3	Group III (Standard Control)	Atenolol (10 mg/kg, <i>s.c</i> ) + (ISP) <i>s.c</i> 85mg/kg on last 2 days	49.03±1.77 <sup>***</sup>	136.22±1.30 <sup>***</sup>
4	Group IV (Plant Extract Low Dose)	MEBA (100 mg/kg <i>p.o.</i> ) + ISP <i>s.c</i> (85 mg/kg) on last 2 days	43.36±0.75 <sup>***</sup>	133.06±0.78 <sup>***</sup>
5	Group V (Plant Extract High Dose)	MEBA (200 mg/kg <i>p.o.</i> ) + ISP <i>s.c</i> (85 mg/kg) on last 2 days	49.15±2.58 <sup>***</sup>	136.79±1.37 <sup>***</sup>

Values are expressed as mean ± SD (n=6), where \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , significant reduction in group III, IV&V compared to group II as compared to diseased control; where # $p < 0.05$ , ## $p < 0.01$ , ### $p < 0.001$ , # significant reduction in group II compared to group I.

**Table 2.** Effect of methanolic extract of *Basella alba* against ISP induced MI on heart tissue homogenate levels of CPK and LDH.

S.No	Groups	Treatment Schedule	CPK(IU/L)	LDH(IU/L)
1	Group I (Normal Control)	Distilled water (2.5 ml/kg)	49.96±0.93	123.39±1.61
2	Group II (Negative Control)	Isoproterenol (ISP) <i>s.c</i> 85mg/kg on last 2 days	30.45±1.03 <sup>#</sup>	99.45±0.62 <sup>#</sup>
3	Group III (Standard Control)	Atenolol (10 mg/kg, <i>s.c</i> ) + (ISP) <i>s.c</i> 85mg/kg on last 2 days	48.06±0.57 <sup>***</sup>	133.00±1.43 <sup>***</sup>
4	Group IV (Plant Extract Low Dose)	MEBA (100 mg/kg <i>p.o.</i> ) + ISP <i>s.c</i> (85 mg/kg) on last 2 days	42.33±0.48 <sup>***</sup>	125.07±1.53 <sup>***</sup>
5	Group V (Plant Extract High Dose)	MEBA (200 mg/kg <i>p.o.</i> ) + ISP <i>s.c</i> (85 mg/kg) on last 2 days	46.15±1.04 <sup>***</sup>	130.45±0.47 <sup>***</sup>

Values are expressed as Mean ± SD (n=6), where \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , significant reduction in group III, IV&V compared to group II as compared to diseased control; where # $p < 0.05$ , ## $p < 0.01$ , ### $p < 0.001$ , # significant reduction in group II compared to group I.

**Table 3.** Effect of methanolic extract of *Basella alba* against ISP induced MI on serum levels of AST and ALT

S.No	Groups	Treatment Schedule	AST(IU/L)	ALT(IU/L)
1	Group I (Normal Control)	Distilled water (2.5 ml/kg)	96.40±1.38	64.58±0.88
2	Group II (Negative Control)	Isoproterenol (ISP) <i>s.c</i> 85mg/kg on last 2 days	210.40±1.21 <sup>#</sup>	173.20±0.62 <sup>#</sup>
3	Group III (Standard Control)	Atenolol (10 mg/kg, <i>s.c</i> ) + (ISP) <i>s.c</i> 85mg/kg on last 2 days	99.16±0.66 <sup>***</sup>	66.76±0.60 <sup>***</sup>
4	Group IV (Plant Extract Low Dose)	MEBA (100 mg/kg <i>p.o.</i> ) + ISP <i>s.c</i> (85 mg/kg) on last 2 days	93.35±1.57 <sup>***</sup>	67.51±1.28 <sup>***</sup>
5	Group V (Plant Extract High Dose)	MEBA (200 mg/kg <i>p.o.</i> ) + ISP <i>s.c</i> (85 mg/kg) on last 2 days	99.15±0.63 <sup>***</sup>	65.93±1.05 <sup>***</sup>

Values are expressed as Mean ± SD (n=6), where \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , significant reduction in group III, IV&V compared to group II as compared to diseased control; where # $p < 0.05$ , ## $p < 0.01$ , ### $p < 0.001$ , # significant reduction in group II compared to group I.

The significant acute MI was indicated by the elevated levels of total cholesterol (CH), triglycerides (TGL) and low-density lipoproteins (LDL) in Group II. In the treated groups IV and V, the levels were reduced to levels closest to the normal values, because of the action of plant extract. The results were significantly comparable with the standard group III. The levels of HDL reduced to  $24.12 \pm 1.16$  in ISP induced group, reflecting the reduction of good cholesterol. But in the treated groups IV ( $36.43 \pm 0.71$ ) and V ( $32.68 \pm 1.42$ ) the HDL level increased significantly which is comparable with the Group III ( $32.95 \pm 0.88$ ) (Table 4).

The methanolic extract of *Basella alba* affects antioxidant enzymes like MDA, SOD and CAT in both serum levels and heart tissue homogenate. Malondialdehyde is one of the many products of lipid peroxidation. In the present investigation, we observed a

significant elevation in MDA levels of both serum and heart tissue homogenate,  $230.60 \pm 1.66$  and  $130.60 \pm 1.09$  in the ISP induced group II as compared to the control group I, which showed values of  $109.50 \pm 13.22$  and  $99.50 \pm 0.94$ . The results clearly depict the injured state of myocardium following ischemia-reperfusion injury. The treatment with methanolic extract of *Basella alba* for 30 days orally, elevated the MDA level in serum and heart tissue significantly compared to control animals. The levels of CAT and SOD showed a significant decrease in the value of Group II compared to Group I. But treatment with the plant extract significantly elevated the levels of CAT and SOD in both serum and heart tissue homogenate (Tables 5 and 6).

Results of the histopathological studies for the treatment period of 30 days are presented in Figure 1.

**Table 4.** Effect of methanolic extract of *Basella alba* against ISP induced MI on serum levels of CH, TGL, HDL and LDL

S.No	Groups	Treatment Schedule	Cholesterol (CH) (mg/dl)	TGL (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
1	Group I (Normal Control)	Distilled water (2.5 ml/kg)	96.40±1.38	64.58±0.88	33.90±1.44	64.58±0.94
2	Group II (Negative Control)	Isopreterenol (ISP) s.c 85mg/kg on last 2 days	210.40±1.21 <sup>#</sup>	173.20±0.62 <sup>##</sup>	24.12±1.16 <sup>#</sup>	173.20±1.70 <sup>##</sup>
3	Group III (Standard Control)	Atenolol (10 mg/kg, s.c) + (ISP) s.c 85mg/kg on last 2 days	99.16±0.66 <sup>***</sup>	66.76±0.60 <sup>***</sup>	32.95±0.88 <sup>***</sup>	66.76±1.29 <sup>***</sup>
4	Group IV (Plant Extract Low Dose)	MEBA (100 mg/kg p.o.)+ ISP s.c (85 mg/kg) on last 2 days	93.35±1.57 <sup>***</sup>	67.51±1.28 <sup>***</sup>	36.43±0.71 <sup>***</sup>	67.51±1.34 <sup>***</sup>
5	Group V (Plant Extract High Dose)	MEBA (200 mg/kg p.o.)+ ISP s.c (85 mg/kg) on last 2 days	99.15±0.63 <sup>***</sup>	65.93±1.05 <sup>***</sup>	32.68±1.42 <sup>***</sup>	65.93±0.88 <sup>***</sup>

Values are expressed as Mean ± SD (n=6), where \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , significant reduction in group III, IV&V compared to group II as compared to diseased control; where #  $p < 0.05$ , ## $p < 0.01$ , ### $p < 0.001$ , # significant reduction in group II compared to group I.

**Table 5.** Effect of methanolic extract of *Basella alba* against ISP induced MI on serum levels of CAT, MDA and SOD

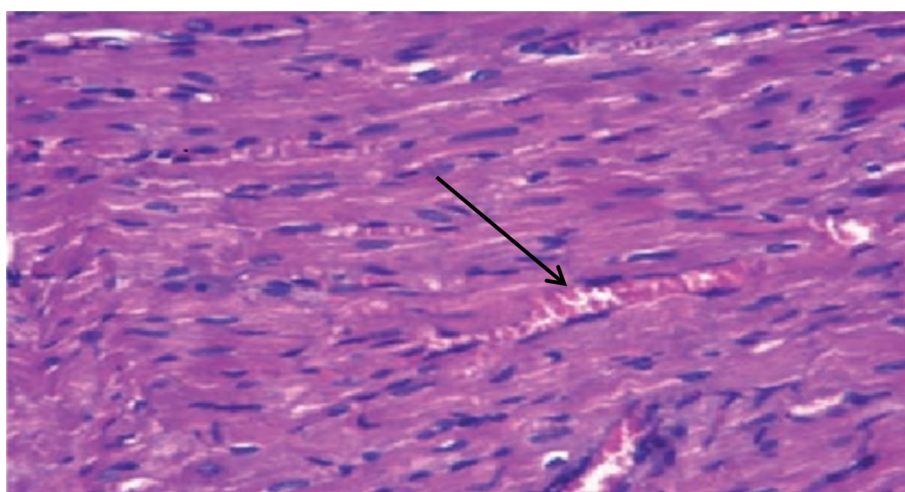
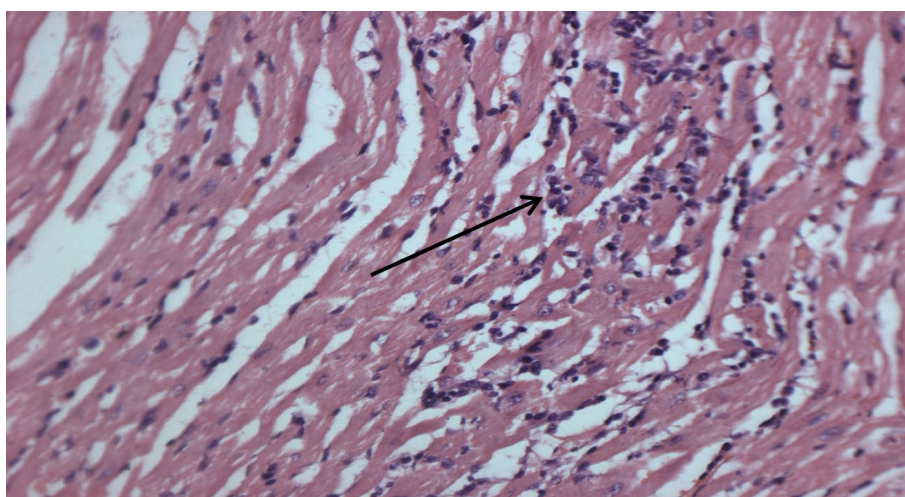
S.No	Groups	Treatment Schedule	CAT units/ml	MDA nmol/dl	SOD units/ml
1	Group I (Normal Control)	Distilled water (2.5 ml/kg)	1.07±0.08	109.50±13.22	4.33±0.38
2	Group II (Negative Control)	Isopreterenol (ISP) s.c 85mg/kg on last 2 days	0.55±0.11 <sup>#</sup>	230.60±1.66 <sup>##</sup>	1.77±0.54 <sup>##</sup>
3	Group III (Standard Control)	Atenolol (10 mg/kg, s.c) + (ISP) s.c 85mg/kg on last 2 days	1.28±0.19 <sup>***</sup>	92.66±1.41 <sup>***</sup>	4.22±0.48 <sup>***</sup>
4	Group IV (Plant Extract Low Dose)	MEBA (100 mg/kg p.o.)+ ISP s.c (85 mg/kg) on last 2 days	1.25±0.30 <sup>***</sup>	121.80±1.65 <sup>***</sup>	2.27±0.87 <sup>***</sup>
5	Group V (Plant Extract High Dose)	MEBA (200 mg/kg p.o.)+ ISP s.c (85 mg/kg) on last 2 days	0.82±0.32 <sup>***</sup>	101.83±1.57 <sup>***</sup>	3.05±0.59 <sup>***</sup>

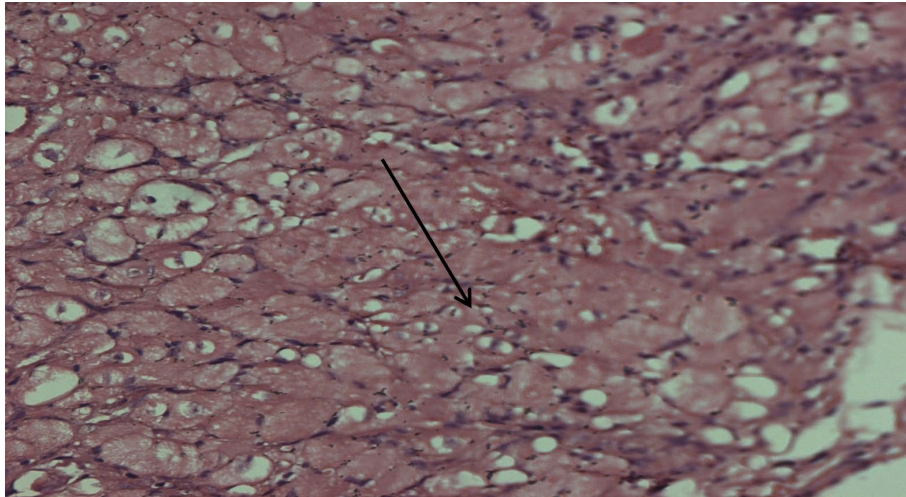
Values are expressed as Mean ± SD (n=6), where \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , significant reduction in group III, IV&V compared to group II as compared to diseased control; where #  $p < 0.05$ , ## $p < 0.01$ , ### $p < 0.001$ , # significant reduction in group II compared to group I.

**Table 6.** Effect of methanolic extract of *Basella alba* against ISP induced MI on heart tissue homogenate levels of CAT, MDA and SOD.

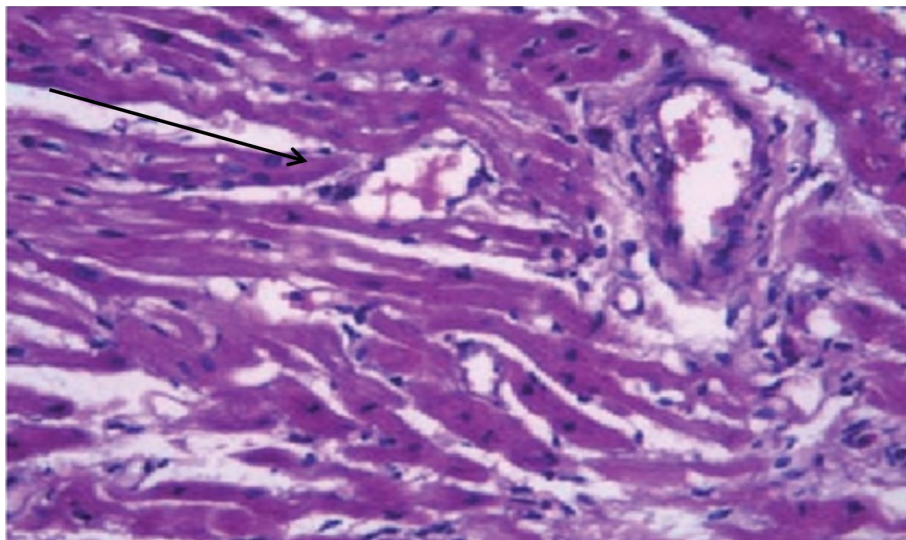
S.No	Groups	Treatment Schedule	CAT units/ml	MDA nmol/dl	SOD units/ml
1	Group I (Normal Control)	Distilled water (2.5 ml/kg)	1.67±0.30	99.50±0.94	4.11±0.13
2	Group II (Negative Control)	Isoproterenol (ISP) <i>s.c</i> 85mg/kg on last 2 days	0.32±0.11 <sup>##</sup>	130.60±1.09 <sup>##</sup>	1.05±0.15 <sup>##</sup>
3	Group III (Standard Control)	Atenolol (10 mg/kg, <i>s.c</i> ) + (ISP) <i>s.c</i> 85mg/kg on last 2 days	1.89±0.23 <sup>***</sup>	92.66±2.36 <sup>***</sup>	4.27±0.26 <sup>***</sup>
4	Group IV (Plant Extract Low Dose)	MEBA (100 mg/kg <i>p.o.</i> ) + ISP <i>s.c</i> (85 mg/kg) on last 2 days	0.99±0.16 <sup>***</sup>	121.80±1.64 <sup>***</sup>	2.97±0.19 <sup>***</sup>
5	Group V (Plant Extract High Dose)	MEBA (200 mg/kg <i>p.o.</i> ) + ISP <i>s.c</i> (85 mg/kg) on last 2 days	1.46±0.29 <sup>***</sup>	100.30±3.04 <sup>***</sup>	4.01±0.10 <sup>***</sup>

Values are expressed as Mean ± SD (n=6), where \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , significant reduction in group III, IV&V compared to group II as compared to diseased control; where #  $p < 0.05$ , ## $p < 0.01$ , ### $p < 0.001$ , # significant reduction in group II compared to group I.

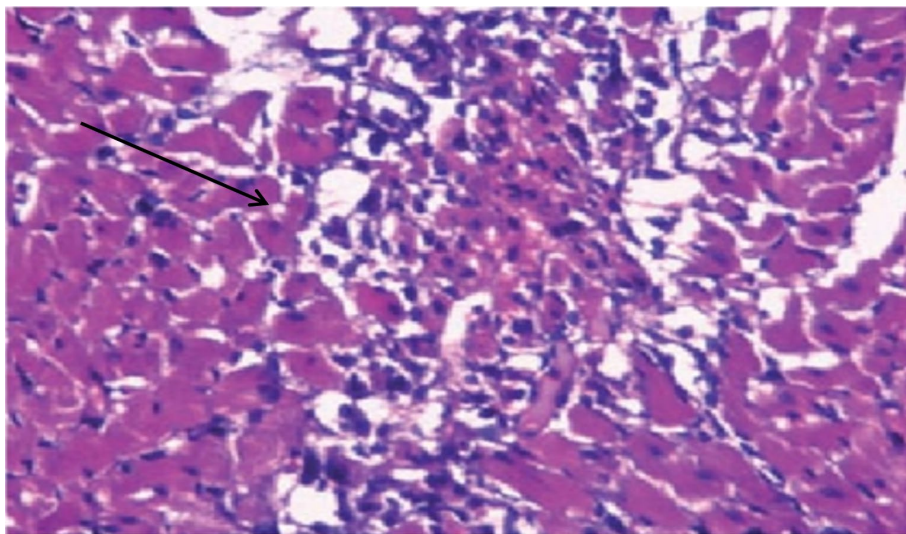
**Group-I:** Normal Control treated with distilled water**Group-II:** Negative Control treated with ISP



**Group-III:** Standard Control treated with Atenolol + ISP



**Group-IV:** Treated with MEBA low dose + ISP



**Group-V:** Treated with MEBA high dose + ISP

**Figure 1.** Effect of methanolic extract of *Basella alba* against ISP induced MI on heart tissue of histopathological studies

## 4. Discussion

Myocardial infarction continues to be the largest cause of mortality worldwide, and quick treatment for a heart attack is critical to survival. Plants have played an important role in the traditional Indian therapeutic system, particularly in terms of cardiovascular protection. Several herbs and herbal products have been recommended for prophylactic and therapeutic effects in reducing cardiovascular diseases (CVDs) and have been reviewed [20, 21]. Isoproterenol, a synthetic non selective  $\beta$ -adrenergic agonist, has been widely used to investigate the effect of drugs on myocardial infarction [22, 23].

In this study, a rat model of myocardial injury (treated with ISP) was confirmed by elevated serum levels of AST, ALT, CPK, LDH and lipid profile, along with abnormal cardiac histopathology. Oxidative stress, driven by free radical formation and a deficit in endogenous antioxidants (SOD, CAT and MDA), likely contributes to myocardial infarction and subsequent heart failure. The plant drugs used demonstrated a high safety index, potentially offering cardioprotective effects by mitigating oxidative damage [24-26].

The heart contains a high concentration of diagnostic marker enzymes such as CPK, LDH, and transaminases (AST and ALT), and when the heart is metabolically injured, its contents are released into the extracellular fluid (ECF). In the present study, it was noted that in ISP myocardial infarcted rats, the increased activities of the serum marker enzymes accompanied by their concomitant reduction in the heart homogenate, confirm the onset of myocardial necrosis. As a result, the total concentration of the marker enzymes was found to be lower in heart tissue of Isoproterenol-treated rats than in control rats, which could be attributed to the effects of cellular injury caused by lipid peroxides. ISP is well known to generate free radicals and to stimulate lipid peroxidation, which may be a causative factor for the irreversible damage to the myocardium [27].

CPK is a muscle-specific enzyme found mostly in the heart and brain; thus, a rise in serum levels is caused by myocarditis, cardiac insufficiency, arrhythmias, and myocardial infarctions. The inhibition of glycolytic pathways of energy in cardiac muscles of isoproterenol-treated rats, leads to glycogen breakdown, loss of pyridine nucleotides and ATP, which results in an increase in intracellular calcium. Decreased activities of these enzymes were due to the leakage from the damaged heart tissues into the blood stream as a result of necrosis induced by isoproterenol in rats. It is observed that these cardio specific marker enzymes are released from the heart into the blood during myocardial damage due to myofibril degeneration and myocyte necrosis. A significant increase was noticed in the activities of cardiac markers like LDH and CPK in plasma of isoproterenol-treated rats, which is consistent with earlier reports. It might be due to enhanced

susceptibility of myocardial cell membrane to the isoproterenol-mediated peroxidative damage, resulting in increased release of these diagnostic marker enzymes into the systemic circulation [28-31].

Transaminase (AST and ALT) levels are sensitive indicators of liver cell injury and are also helpful in recognizing other diseases. AST is found in decreasing order of concentration in the liver, cardiac muscle, skeletal muscle, kidney, brain, pancreas, lungs, leucocytes and erythrocytes. ALT is highly concentrated in the liver and is less specific to other muscle injuries. When tissues are injured, both enzymes are released into the body in greater quantities. Despite being a sensitive indicator of liver cell injury, the transaminases also correlate poorly with severity of cardiac disease [32-35]. Myocardial infarction induced by isoproterenol in male Wistar rats leads to significant alterations in transaminase levels. The effect could be due to the stabilization of heart membrane by methanolic extract of *Basella alba* (MEBA) with a consequent decrease in the leakage of these marker proteins. The tendency of these enzymes to return to near normal in extract administered group is a clear manifestation of the cardioprotective activity of the extract.

The lipid profile, which includes total cholesterol, triglycerides, HDL, and LDL cholesterol, is essential for assessing cardiovascular disease (CVD) risk. Total cholesterol includes "good" HDL and "bad" LDL cholesterol. Elevated total and LDL cholesterol levels contribute to atherosclerosis, a condition where arteries narrow and harden, increasing the risk of heart attacks and strokes. Triglycerides, another form of blood fat, also raise CVD risk, especially when combined with low HDL or high LDL levels. HDL cholesterol, known as "good" cholesterol, helps remove excess cholesterol, lowering CVD risk [36, 37]. In isoproterenol (ISP)-induced myocardial infarction (MI) animals, lipid profile levels were significantly disrupted. However, treatment with the MEBA restored these levels, suggesting its cardioprotective properties.

Lipid peroxidation is a primary mechanism of tissue damage caused by free radicals, with lipids being particularly vulnerable to oxidative stress. Free radicals can peroxidize polyunsaturated membrane lipids, leading to structural and functional damage. Three critical components in understanding oxidative stress and its impact on myocardial infarction (MI) are SOD, CAT, and MDA. SOD is an essential antioxidant enzyme that converts superoxide radicals into oxygen and hydrogen peroxide, reducing oxidative stress and protecting cells. In MI, adequate SOD levels are crucial to minimize heart tissue damage. CAT works alongside SOD by converting hydrogen peroxide, a byproduct of SOD activity, into water and oxygen, preventing its harmful accumulation. Proper CAT function is vital for reducing oxidative stress and safeguarding cardiac tissues during and after MI. MDA is a marker of lipid peroxidation, which indicates oxidative

stress and membrane damage. Elevated MDA levels during MI indicate significant oxidative damage, contributing to heart function deterioration and injury progression [38-43].

Treatment with free radical scavengers has been shown to reduce infarct size in myocardial ischemia and reperfusion, supporting the idea that oxidative stress plays a significant role in reperfusion injury, such as that induced by ISP. Naturally occurring antioxidants, like those found in plant extracts, may help mitigate this damage. The methanolic extract of *Basella alba* has demonstrated moderate antioxidant properties, restoring enzymatic levels in ISP-treated animals, suggesting its potential as a cardioprotective agent by reducing oxidative stress and preserving heart function.

The histopathological analysis of myocardial tissues provided crucial insights into the cardioprotective effects of MEBA against ISP-induced myocardial infarction MI in rats. Control rats exhibited normal myocardial architecture, with well-organized myocardial fibers and clear striations, indicating the absence of any pathological changes such as degeneration or necrosis. In contrast, ISP-induced rats displayed significant pathological alterations, including myocardial congestion, subendocardial necrosis, hyperplasia, and increased edematous intramuscular space, confirming the establishment of MI. However, treatment with MEBA at both 100 mg/kg and 200 mg/kg dosages demonstrated a protective effect on the heart tissues. The hearts of rats treated with MEBA showed a near-normal appearance with only mild changes in congestion and necrosis, comparable to those treated with the standard drug. This suggests that MEBA effectively mitigates the pathological changes induced by ISP, thereby offering cardioprotective benefits.

The cardioprotective effects of MEBA can be attributed to its rich phytochemical composition, as revealed by conventional phytochemical analysis. The presence of bioactive compounds such as alkaloids, flavonoids, phenols, tannins, saponins, and terpenoids in MEBA is particularly noteworthy. These phytoconstituents are known to possess various pharmacological properties, including antioxidant, anti-inflammatory, and vasodilatory effects, which contribute to their cardioprotective potential. The combination of these phytoconstituents in MEBA likely works synergistically to combat the multifaceted pathophysiological processes involved in MI, such as oxidative stress, inflammation, and lipid peroxidation. By restoring enzymatic levels, reducing histopathological damage, and improving overall cardiac function, MEBA demonstrates a promising potential as a natural therapeutic agent for the prevention and management of myocardial infarction.

This study underscores the potential of *Basella alba* methanolic extract as a cardioprotective agent, capable of mitigating the deleterious effects of isoproterenol-induced myocardial infarction. The presence of bioactive phytoconstituents in MEBA contributes to its efficacy in

reducing oxidative stress, improving lipid profiles, and protecting myocardial tissues from necrosis and degeneration. Further studies focusing on the molecular mechanisms and clinical efficacy of *Basella alba* are warranted to validate its use as a natural alternative or complementary therapy in cardiovascular disease management.

## 5. Conclusion

The methanolic extract of *Basella alba* demonstrates significant potential for mitigating the cardiotoxic effects induced by isoproterenol, suggesting its viability as a preventive treatment for myocardial infarction.

The active constituents of *Basella alba* leaves like bioactive compounds, such as flavonoids, alkaloids, phytosterols, tannins, triterpenoids, betacyanins, carotenoids, organic acids, Basellasapins A, B, C, and D, and Kaempherol, contribute to its potential health benefits, including antioxidant, anti-inflammatory, and cardioprotective effects. Ongoing research aims to further elucidate these compounds and their specific roles in promoting health and preventing disease, particularly in the context of cardiovascular health. As interest in natural remedies grows, characterizing these active constituents will be essential for developing standardized extracts for therapeutic use. Iron, calcium, and magnesium are vital minerals present in *Basella alba* contributing to various aspects of heart health. They support oxygen delivery, muscle contraction, heart rhythm regulation, vascular health, and metabolic processes.

As the demand for natural therapies continues to rise, it becomes increasingly important to develop standardized plant extracts that meet established criteria for quality, safety, and efficacy. This necessitates targeted research aimed at elucidating the chemical and pharmacological profiles of *Basella alba*, both as a standalone treatment and in combination with other therapeutic agents.

Such investigations are critical for optimizing the therapeutic applications of *Basella alba* and advancing its status as a reliable natural intervention for cardiovascular diseases. By establishing a robust framework for its efficacy and safety, these efforts could pave the way for the integration of *Basella alba* into conventional treatment paradigms for heart-related ailments, ultimately benefiting patient care and outcomes in the domain of cardiovascular health.

## Acknowledgements

We would like to express our sincere gratitude to Seven Hills College of Pharmacy (Autonomous), Tirupati, AP and Toxgene AR Biolabs Pvt Ltd, Tiruapti, AP, for providing the necessary resources and support to carry out this research.

## Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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