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Cardioprotective effects of hydroalcoholic extract from *Cinnamomum zeylanicum* stem bark against isoproterenol-induced myocardial infarction in rats

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Abstract

Background: The pharmacological properties of *Cinnamomum zeylanicum* have been predominantly explored in the context of cardiovascular diseases. Given its well-established anti-inflammatory and antioxidant properties, this study aimed to evaluate the cardioprotective potential of the hydroalcoholic extract of *Cinnamomum zeylanicum* barks (HECZ) against isoproterenol (ISO) induced cardiotoxicity.
Methods: Rats were pre-treated with HECZ (200 - 400 mg/kg, *p.o.*) or 100 mg/kg of vitamin E for 28 consecutive days, followed by ISO administration (85 mg/kg, *s.c.*) on days 29 and 30. Hemodynamic, hematological, biochemical, and histological parameters were assessed.
Results: Administration of ISO resulted in significant reductions in blood pressure and cardiac antioxidant enzyme activities, along with increased leukocyte counts, enhanced lipid peroxidation, and marked alterations in cardiac marker enzyme levels. This was accompanied by an elevated heart rate, altered serum lipid profiles, increased levels of IL-6, TNF-α, and IL-1β. Histopathological analysis revealed death of heart cells and inflammation in the ISO group. However, pre-treatment with HECZ or Vitamin E significantly mitigated these ISO-induced alterations. The histopathological findings corroborated the biochemical results.
Conclusion: These findings indicate that HECZ mitigated myocardial injury in ISO-treated rats, showcasing its cardioprotective effects through modulation of cardiac parameters, and its antioxidant and anti-inflammatory properties.

Keywords: Anti-inflammatory; antioxidant; cardioprotection; *Cinnamomum zeylanicum*; Isoproterenol; myocardial injury

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Background

Myocardial infarction (MI), a leading cause of cardiomyocyte death, is characterized by myocardial ischemia–induced cardiomyocyte necrosis resulting from an imbalance between myocardial oxygen demand and coronary blood supply [1]. MI and heart failure account for a substantial proportion of cardiovascular diseases, contributing to approximately one-third to one-half of all cases [2]. While the national prevalence of MI in Cameroon is not well documented, a study at the Cardiac Centre of Elizabeth Catholic General Hospital, Shisong, indicated a 0.9% MI prevalence among 8389 adult patients diagnosed with heart diseases between November 2009 and November 2011 [3]. Furthermore, Cameroon's arterial hypertension prevalence was 30.9% by 2019 [4], posing a substantial risk factor for MI.

In managing MI, rapid reperfusion strategies are critical to minimize cardiomyocyte damage. However, reperfusion therapy can induce injury, partly due to free radical generation [5, 6]. Conventional MI treatments, despite their effectiveness, are not universally accessible due to high costs and adverse effects, including dry cough, dizziness, loss of appetite, fatigue, headache, and hyperkalemia. Consequently, herbal medicines have gained attention as viable alternatives, offering cultural acceptance, reduced side effects, and affordability [7, 8]. Traditional medicine use exceeds 75% in many regions, particularly in low-income countries, supporting the exploration of herbal remedies for cardiovascular diseases.

Isoproterenol (β-adrenergic agonist synthetic) is widely employed to cause experimental MI in laboratory animals. The resultant cardiac dysfunctions closely mimic human MI pathology [9]. High doses of ISO trigger increased chronotropism, inotropism, oxidative stress, and inflammation, making it a standard model for evaluating cardioprotective agents [10]. Medicinal plants with antihypertensive, antithrombotic, anti-inflammatory, antihyperlipidemic and antioxidant properties are of particular interest in MI management.

Cinnamomum zeylanicum (Lauraceae family), is a generally used culinary spice with notable pharmacological activities. Experimental studies have demonstrated its antidiabetic [11], nephroprotective [12–14], anti-tumor [15], antidepressant [16], anti-inflammatory [17,18], and immunomodulatory [19] effects. Oxidative stress, a key factor in MI pathogenesis, can be mitigated by *C. zeylanicum*'s antioxidant and free radical scavenging properties [20,21]. Additionally, its hypotensive, antihypertensive, vasorelaxant, hypolipidemic, and antiatherosclerotic activities [22–25] contribute to its cardioprotective potential. Although the cardioprotective effects of *C. zeylanicum*'s aqueous extract have been reported in a doxorubicin-induced cardiotoxicity model [26], its effects against MI (induced by ISO) remain unexplored. This study aimed to evaluate the cardioprotective effect of the hydroalcoholic extract of *Cinnamomum zeylanicum* barks (HECZ) in an isoproterenol (ISO) induced model of myocardial infarction, assessing a broad spectrum of parameters including hemodynamic metrics, electrocardiogram profiles, lipid profiles, cardiac enzyme markers, oxidative stress markers, anti-inflammatory effects, and histopathological changes.

Methods

Plant Materials

Cinnamomum zeylanicum bark was collected in August 2018 from Njombe, Littoral Region, Cameroon, and authenticated by Professor Louis Zapfack (Faculty of Science) using voucher specimen SRFC/22309 deposited at the Cameroon National Herbarium. The harvested bark was cut into small pieces and air-dried at room temperature away from direct sunlight, then ground into a fine powder. The resulting powder (500 g) was macerated in 5 L of a hydroalcoholic solution (70% ethanol and 30% water) for 48 h. The mixture was subsequently filtered using Whatman No. 3 filter paper, and the filtrate was concentrated under reduced pressure to obtain 36 g of hydroalcoholic extract, corresponding to a 7.2% yield.

Experimental animals

Thirty-six male Wistar rats (10–12 weeks old, 150–200 g) were obtained from the animal facility of the Laboratory of Animal Physiology, Faculty of Science, University of Yaoundé I, Cameroon. The rats were kept under normal laboratory environments with normal light cycles, receiving standard feed and water *ad libitum*. All procedures involving animals adhered to the ethical procedures of the Institutional Ethics Committee of the Cameroon Ministry of Scientific Research and Innovation, which comply with the European Union standards for animal care (EEC Council 86/609).

Induction of myocardial infarction

Isoproterenol (CAS RN: 51-30-9, TCI, Japan) was newly prepared in 0.9% NaCl and 85 mg/kg was administered subcutaneously on days 29 and 30 (24-hour interval between injections). The Wistar rats were sacrificed 24 hours after the final isoproterenol injection [27].

Experimental design

The rats were randomly separated into six groups (six Wistar rats per group). Prior to myocardial infarction induction, pretreatment was administered orally for 28 consecutive days:

- Normal control group: distilled water (1 mL/100 g, *b.w.*)
- Isoproterenol (ISO) group: distilled water
- Tocopherol group: 100 mg/kg
- *Cinnamomum zeylanicum* extract groups: 200 mg/kg and 400 mg/kg
- Extract only group: 400 mg/kg without isoproterenol

Body weights were monitored every two days. On days 29 and 30, all groups except the normal control and the extract-only group received isoproterenol injections. These two groups received distilled water or the extract (400 mg/kg), followed by normal saline (0.9% NaCl). The doses of the extract were chosen according to a previous study [14].

Measurement of blood pressure, heart rate, and electrocardiogram

On day 31, rats were anesthetized (15% urethane, 1.5 g/kg, *i.p.*). The trachea was intubated to simplify spontaneous breathing. A polyethylene catheter was introduced into the carotid artery, and needle electrodes were positioned subcutaneously in a lead II

configuration. These were connected to a Biopac Student Lab MP35 system (USA) to measure HR (heart rate), BP (blood pressure), and ECG (electrocardiogram) after a 30-minute equilibration period [28].

Hematological and biochemical analysis, and heart sample collection

Following hemodynamic measurements, blood samples were collected (in carotid artery) into tubes with and without anticoagulant (EDTA) for hematological and biochemical assessments. Rats were then euthanized, and their hearts were excised, weighed, and processed to assess cardiac hypertrophy.

Hematological parameters were analyzed using a Mindray BC-3000 auto hematology analyzer, including hematocrit, red blood cell, mean corpuscular volume, white blood cell, hemoglobin, platelet, mean corpuscular hemoglobin concentration and mean corpuscular hemoglobin count.

Biochemical analyses included serum markers of heart tissue injury (LDH, AST, CK-MB, ALT, ALP) and total protein levels [29]. . Lipid profile parameters (HDL, total cholesterol, LDL, triglycerides,) were also measured, and atherogenic and coronary risk indices were calculated [30]. The heart tissue was divided into oxidative stress, cytokine analysis and histopathological evaluation.

Oxidative stress assessment

Heart tissues were homogenized (Tris-KCl buffer, pH 7.4)) to prepare homogenates (20%, w/v). After centrifugation (1160g, 4°C, 15 min) and collect supernatant, this was kept (-20°C) for subsequent analyses. Superoxide dismutase (SOD) [31], catalase (CAT) [32], reduced glutathione (GSH) [33].and malondialdehyde (MDA) [34]. levels were measured using established spectrophotometric methods.

Inflammatory marker quantification

Cardiac tissue homogenates were analyzed for IL-6, IL-1β, TNF-α using R&D Systems, USA ELISA kits [35] . Nitric oxide (NO) levels were quantified using the Griess method, with absorbance measured at 540 nm [36].

Histopathological evaluation

Heart tissues were fixed (formalin buffered 10%), embedded (paraffin), and sectioned (5 µm) slices using a Reichert-Jung microtome. Pieces were soaked in H&E (hematoxylin/eosin) and observed (light microscope) for myocardial necrosis and inflammation. Lesions were scored on a scale from 0 (no changes) to 3 (marked damage) based on the extent of inflammatory infiltration and/or myocardial degeneration.

Statistical analysis

Data were presented (mean ± SEM) for each group (n=6). Statistical analyses were made using one-way ANOVA followed by Tukey's test for multiple comparisons. The analysis was conducted using GraphPad Prism version 8.01, with a significance threshold set at $P < 0.05$.

Results

Cardiac hypertrophy is reduced and body weight is not affected by HECZ

No significant ($p>0.05$) alterations in body weight were perceived among all treatment groups, indicating that none of the interventions affected overall body mass. However, isoproterenol (ISO) administration significantly increased ($p<0.001$) both total heart weight and the heart weight-to-body weight ratio compared to the control group, highlighting the progress of cardiac hypertrophy. Notably, treatment with the hydroalcoholic extract of *C. zeylanicum* (HECZ) or Vitamin E (VIT E) effectively mitigated these increases, demonstrating a significant reduction in both heart weight and the heart weight-to-body weight ratio relative to the ISO-only treated group (Table 1).

Hemodynamic stabilization and ECG improvement with HECZ treatment

ISO exposure led to a marked reduction in hemodynamic parameters, including SBP (systolic blood pressure), DBP (diastolic blood pressure), and MABP (mean arterial blood pressure) when related to the normal or control group. Specifically, MABP decreased by 29.11% ($p<0.001$) in the ISO group. Pre-treatment with VIT E, HECZ at 200 mg/kg, or HECZ at 400 mg/kg significantly improved MABP by 39.33% ($p<0.001$), 32.02% ($p<0.001$), and 30.39% ($p<0.001$), respectively. Conversely, in the group treated with HECZ (400 mg/kg) alone, MABP revealed a significant decrease of 20.44% ($p<0.001$) compared to the control.

The heart rate also showed a significant increase in the ISO group, rising by 8.98% ($p<0.01$) from 376.00 ± 7.28 bpm in the control group to 409.80 ± 3.73 bpm. Pre-treatment with VIT E or HECZ at both 200 mg/kg and 400 mg/kg for 28 days significantly reduced heart rate by 7.51% ($p<0.05$), 7.56% ($p<0.05$), and 8.50% ($p<0.01$), respectively, when compared to the ISO group (Table 2).

ECG analysis on day 30 revealed that ISO administration significantly ($p<0.001$) altered ECG patterns, showing decreased QRS amplitude and elevated ST segments. Treatment with HECZ at both doses or with VIT E notably improved ECG parameters, as evidenced by increased QRS complex ($p<0.05$, $p<0.01$) and reduced ST segment elevation ($p<0.001$) relative to the ISO group.

Hematological parameters restored to normal with HECZ

Table 3 outlines the influence of HECZ on hematological parameters. ISO treatment caused a significant increase ($p<0.01$) in white blood cell (WBC) count, reflecting an inflammatory response. However, VIT E and HECZ (200 and 400 mg/kg) effectively normalized WBC levels to those comparable to the control group. No other hematological parameters exhibited significant changes regardless of the treatment received.

Lipid profiles improved by HECZ treatment

Table 4 presents data on lipid parameters, including TC (total cholesterol), TG (triglycerides), HDL-C (high-density lipoprotein cholesterol), LDL-C (low-density lipoprotein cholesterol), and the atherogenic index (AI). ISO intoxication significantly elevated serum TC, AI, LDL-C, TG, and coronary risk index (CRI) while reducing HDL-C compared to control rats. Pre-treatment with HECZ for 28 days significantly reduced ($p<0.001$) TC, AI, LDL-C, TG, and CRI, while increasing HDL-C levels. VIT E treatment

similarly maintained lipid profiles within a near-normal range, mirroring the effects of HECZ. Additionally, a standalone HECZ treatment at 400 mg/kg led to a significant reduction ($p<0.05$, $p<0.01$) in TC and TG levels.

Prevention of blood and heart protein levels declines by HECZ

ISO exposure led to significant reductions in both plasma protein (29.27%) and cardiac protein levels (50.42%) compared to the control group. Pre-treatment with HECZ (200 and 400 mg/kg) significantly prevented these declines, increasing proteinemia by 37.6% and 41.2%, respectively, and enhancing heart protein content by 81.60% ($p<0.01$) and 127.01% ($p<0.001$) compared to the ISO group (Figure 1).

Myocardial enzyme levels in serum reduced by HECZ

ISO administration caused significant elevations in serum levels of ASAT (64.06%, $p<0.001$), ALAT (37.37%, $p<0.01$), LDH (55.65%, $p<0.001$), CK-MB (47.47%, $p<0.001$), and ALP (15.58%, $p<0.05$). However, pre-treatment with HECZ or VIT E significantly attenuated these increases, maintaining enzyme levels close to those of the control group. Notably, NO and cytokine levels remained unaltered in the HECZ-only treated group (Figure 2).

Oxidative stress and inflammatory markers alleviated by HECZ

Table 5 illustrates the impact of HECZ on MDA, CAT, SOD, and GSH. ISO-induced myocardial infarction caused a substantial increase in MDA levels ($p<0.001$) and a significant decrease ($p<0.05$; $p<0.001$) in SOD, CAT, and GSH activities. Pre-treatment with VIT E or HECZ significantly reversed these changes, aligning oxidative stress marker levels with those of the control group.

TNF-α, IL-1β, IL-6, and NO levels in cardiac homogenates, were significantly elevated ($p<0.001$) following ISO treatment. However, dose-dependent pre-treatment with HECZ (200 and 400 mg/kg) or VIT E effectively reduced these inflammatory markers, showing no significant differences compared to the normal control in the HECZ 400 mg/kg group.

Myocardial structure preserved by HECZ treatment

Histopathological analysis (Figure 3) revealed that control and HECZ-only treated rats displayed normal myocardial architecture without leukocyte infiltration or necrosis. Conversely, ISO-treated rats showed significant myocardial damage, characterized by inflammatory foci, edema, cardiomyocyte necrosis, and a significantly high histopathological score ($p<0.001$). Rats pre-treated with HECZ or VIT E before ISO injection exhibited near-normal myocardial histoarchitecture, with a significant reduction ($p<0.001$) in tissue damage compared to the ISO-only group.

Overall, these findings demonstrated that HECZ exerts a cardioprotective effect by modulating hemodynamic parameters, improving lipid profiles, enhancing protein levels, reducing oxidative stress and inflammatory responses, and preserving myocardial structure in ISO-induced rat myocardial infarction.

Discussion

This study aimed to evaluate the effects (cardioprotective) of the hydroalcoholic extract of HECZ in an isoproterenol (ISO)-induced MI (myocardial infarction) model in rats. Both HECZ and Vitamin E treatments effectively mitigated the detrimental impacts of ISO on myocardial tissue, suggesting their potential therapeutic value in managing cardiac injuries.

Isoproterenol (catecholamine and β-adrenergic receptor agonist) is widely used to induce MI in laboratory animals. The pathological and morphological changes observed in the hearts of rats subjected to ISO closely resemble the characteristics of human MI [9]. This experimental model thus provides a relevant platform for assessing potential cardioprotective agents.

In this study, ISO administration resulted in reduced body weight gain and an increased relative heart weight in rats. These findings align with prior studies indicating that ISO may trigger proteolysis and inhibit protein synthesis, contributing to reduced body mass [37]. The decrease in total protein levels observed in both serum and heart tissues of ISO-treated rats further corroborated this hypothesis. Interestingly, HECZ not only prevented ISO-induced weight loss but also promoted higher body weights in treated animals compared to normal controls, indicating its potential role in modulating protein metabolism. The prevention of serum protein depletion by HECZ suggests an inhibitory effect on proteolysis, though the lack of a protein increase in the absence of ISO indicates limited impact on protein synthesis. These results are in line with previous research demonstrating the nephroprotective effects of HECZ against gentamicin-induced renal toxicity in rats [14].

ISO administration is known to disrupt hemodynamic parameters, leading to decreased systolic, diastolic, and mean arterial pressures and an increased heart rate. These changes result from ISO's dromotropic, lusitropic, chronotropic, and positive inotropic effects, which ultimately impair myocardial perfusion and induce cardiac damage [38]. However, treatments with HECZ and Vitamin E significantly ameliorated these hemodynamic disturbances, restoring arterial pressure indices and stabilizing heart rate. This indicates that both interventions offer significant protection to cardiac hemodynamics during ischemic episodes.

Electrocardiogram (ECG) analysis, a critical diagnostic tool for MI, revealed typical abnormalities such as ST-segment elevation and deep Q-wave in ISO-treated rats. These alterations reflect loss of cell membrane integrity and compromised electrical activity in the myocardium [39]. ISO treatment significantly reduced P and QRS wave amplitudes, indicating myocardial necrosis. Conversely, HECZ administration notably improved these ECG parameters, demonstrating its cardioprotective effects. Additionally, HECZ prevented ISO-induced ST-segment elevation, suggesting a membrane-stabilizing effect that supports myocardial integrity.

Dyslipidemia is a known risk factor for cardiovascular diseases, contributing to myocardial damage through altered lipid metabolism and atherosclerosis. In this study, ISO-treated rats exhibited significant increases in serum total cholesterol, triglycerides, atherogenic index, coronary risk index, and LDL cholesterol, alongside a reduction in HDL cholesterol. HECZ treatment effectively normalized these lipid profiles, highlighting its hypolipidemic potential. Preceding studies have revealed that cinnamon bark extract and its active component cinnamate can reduce lipid biosynthesis by inhibiting hepatic HMG-CoA reductase activity, contributing to lower cholesterol and triglyceride levels [40-47].

ISO-induced myocardial injury is also characterized by elevated levels of cardiac biomarkers such as CK-MB, AST, LDH, ALT, and ALP, indicating compromised cell membrane integrity [48-52]. HECZ and Vitamin E treatments significantly reduced these biomarker levels, suggesting the preservation of myocardial cellular structure and limiting enzyme leakage into circulation.

Oxidative stress plays an essential role in ISO-induced cardiac injury through the generation of free radicals. The present study showed decreased antioxidant enzyme activities (SOD, CAT) and reduced non-enzymatic antioxidant (GSH) levels in the hearts of ISO-treated rats, along with increased malondialdehyde (MDA) levels. HECZ treatment enhanced antioxidant defense mechanisms and restored MDA levels to near-normal, supporting its antioxidant properties. These results align with prior findings that indicated HECZ's ability to scavenge lipid peroxidation products and provide myocardial protection [14].

Inflammatory processes significantly contribute to MI pathogenesis. HECZ exhibited anti-inflammatory effects by decreasing cardiac nitric oxide (NO) levels, lowering pro-inflammatory cytokines, and decreasing inflammatory cell infiltration in cardiac tissue. This anti-inflammatory action is consistent with previous studies on the effects of *Cinnamomum zeylanicum* in other models of toxicity and inflammation [14, 53, 54].

Additionally, ISO-induced myocardial infarction caused leukocytosis, a common immune response to inflammation and myocardial necrosis [55]. HECZ administration countered this effect, demonstrating its potential to modulate inflammatory responses. These findings are further supported by histopathological evaluations showing that HECZ treatment maintained myocardial cell integrity, reduced myonecrosis, and diminished inflammatory infiltration in cardiac tissues. The cardioprotective effects of HECZ perceived in this study may be partially credited to cinnamaldehyde, its major bioactive constituent, which has been documented for its antioxidant, anti-inflammatory, and vasorelaxant properties [56-59]. Histological and biochemical findings were well correlated, reinforcing the notion that HECZ treatment offers substantial protection against ISO-induced myocardial damage.

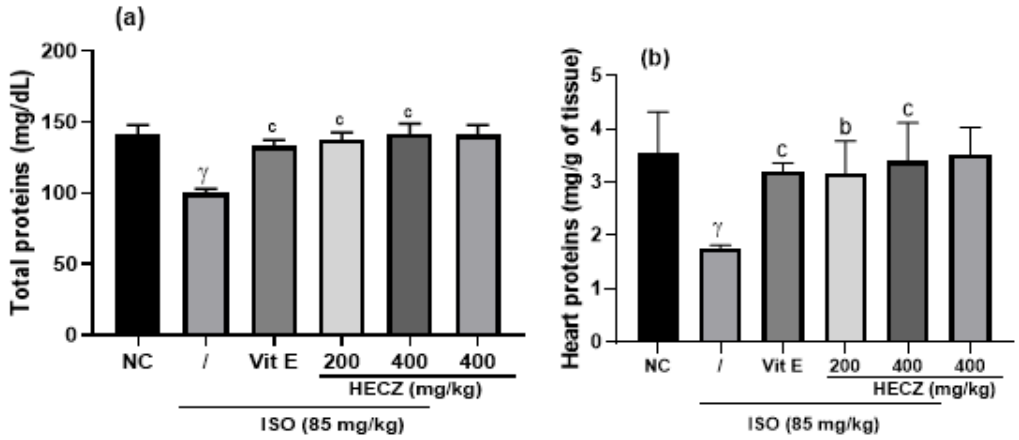

Figure 1. Effects of the hydroalcoholic extract of *Cinnamomum zeylanicum* on blood (a) and heart (b) proteins in Isoproterenol induced myocardial infarction in rats.

Each bar represents the mean ± SEM. n = 6; $^{\gamma}p<0.001$: significant differences as compared to normal control (NC). $^{b}p<0.01$, $^{c}p<0.001$: significant differences as compared to the isoproterenol group (ISO (85 mg/kg)), HECZ: hydroalcoholic extract of *Cinnamomum zeylanicum*, and VIT E = Vitamin E (100 mg/kg)

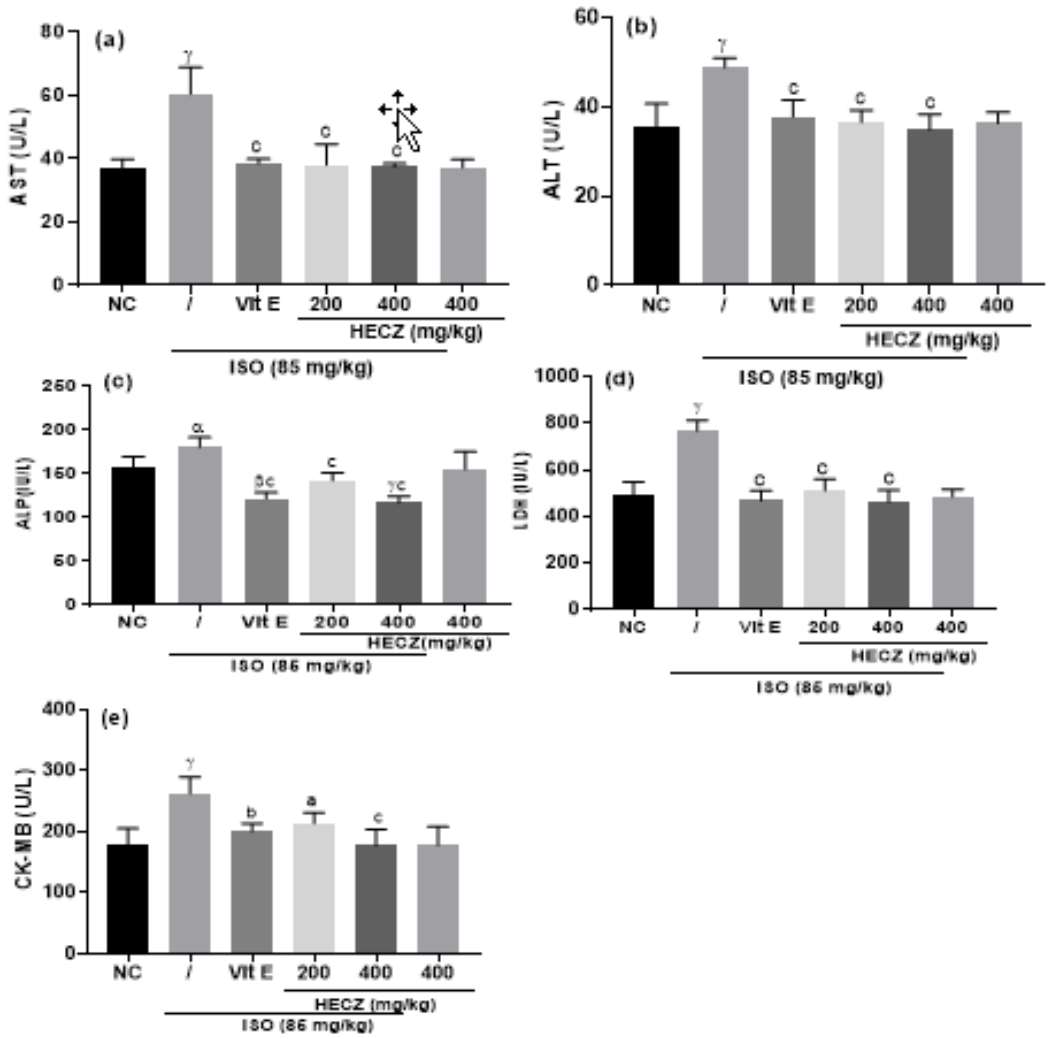

Figure 2. Effects of *Cinnamomum zeylanicum* stem bark hydroalcoholic extract (HECZ) on cardiac maker enzymes.

Each bar represents the mean ± SEM. n = 6; $^{\beta}p<0.01$, $^{\gamma}p<0.001$: significant differences as compared to normal control (NC). $^{a}p<0.05$, $^{b}p<0.01$, $^{c}p<0.001$: significant differences as compared to the isoproterenol group (ISO (85 mg/kg)), HECZ: stem barks hydroalcoholic extract of *Cinnamomum zeylanicum*, and VIT E= Vitamin E (100 mg/kg). AST= aspartate amino-transferase, ALT= alanine amino-transferase, LDH= lactate dehydrogenase, ALP= alkaline phosphatase, CK-MB= creatine kinase- MB

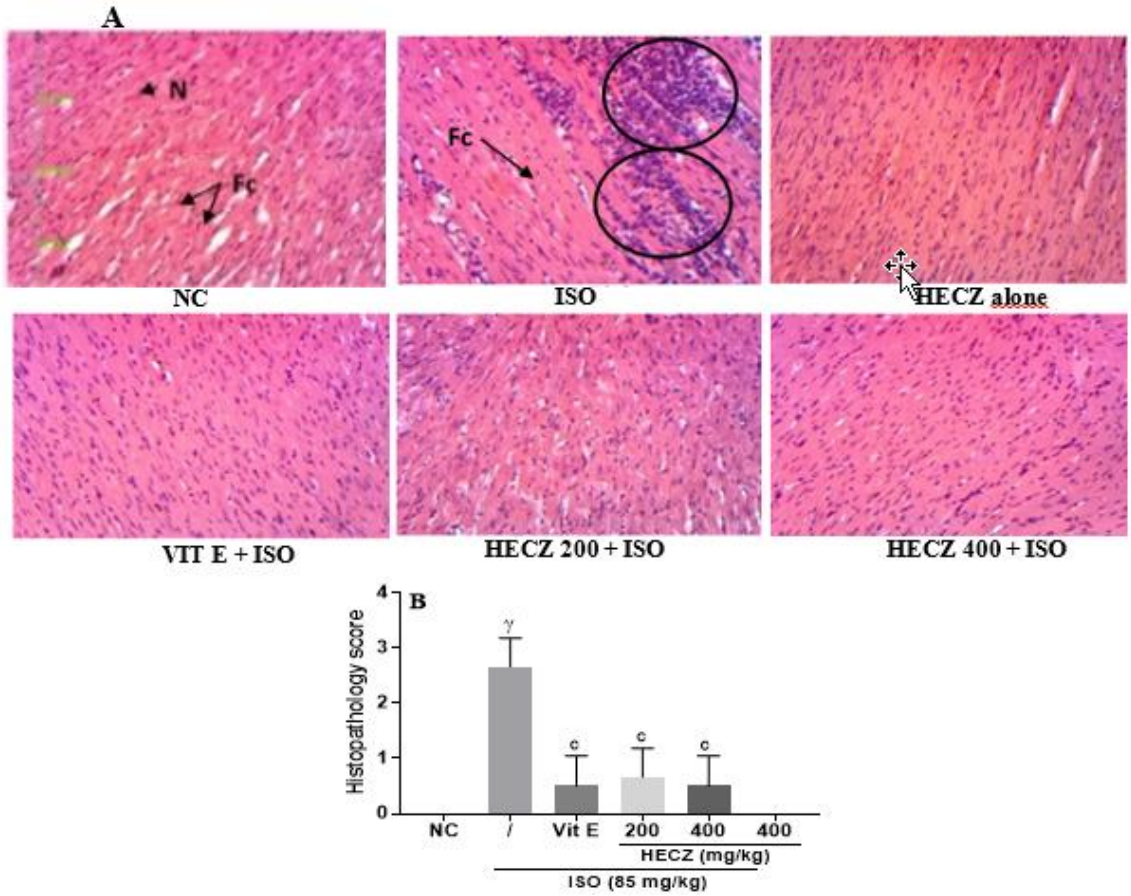

Figure 3. Effects of *Cinnamomum zeylanicum* hydroalcoholic extract (HECZ) on histopathological changes (A) and on histological score (B) in heart tissue.

Each data represents the mean ± SEM. n = 6; $^{\gamma}p$<0.001: significant differences as compared to normal control (NC). ^{c}p<0.001 indicate significant differences as compared to the isoproterenol group. **NC:** Normal control group received saline showing normal structure of myocardium; **ISO:** Diseased group received two subcutaneous injections of isoproterenol (ISO, 85 mg/kg) showing necrosis of myofibrils and large numbers of invasive inflammatory cells; HECZ alone: received only the extract at the dose 400 mg/kg showing normal structure of myocardium; VIT E + ISO: positive control group received vitamin E (100 mg/kg) + two subcutaneous injections of isoproterenol (ISO, 85 mg/kg) showing very slight alterations in cardiac tissue; HECZ 200 mg/kg and HECZ 400 mg/kg + two subcutaneous injections of isoproterenol (ISO, 85 mg/kg) respectively showing lesser myocardial necrosis and decrease in inflammatory foci. Heart tissues were stained with hematoxylin and eosin and visualized under the light microscope at x 100 magnification. **N** = Nuclei of heart muscle fibre; **Fc** = Cardiac muscle fibre; **Circle** = Leukocyte invasion (inflammation-myocarditis) and intense necrotic zon.

Table 1. Effects of the hydroalcoholic extract of *Cinnamomum zeylanicum* on body weight, heart weight and heart weight/body weight ratio in Isoproterenol induced myocardial infarction in rats.

	Body weight at Day 31 (g)	Heart weight (g)	Heart weight/ Body weight ratio (%)
Normal control	240.80 ± 4.57	0.79 ± 0.01	0.33 ± 0.01
ISO	237.20 ± 4.28	1.23 ± 0.03$^{\gamma}$	0.52 ± 0.01$^{\gamma}$
VIT E + ISO	247.80 ± 4.17	0.91 ± 0.02$^{\beta}$	0.36 ± 0.01^{c}
HECZ 200 + ISO	241.40 ± 3.10	0.77 ± 0.01^{c}	0.32 ± 0.00^{c}
HECZ400 + ISO	246.00 ± 4.26	0.74 ± 0.02^{c}	0.30 ± 0.01^{c}
HECZ 400	244.20 ± 4.55	0.78 ± 0.01	0.32 ± 0.01

Each data represents the mean ± SEM. n = 6; $^{\beta}p$<0.01, $^{\gamma}p$<0.001: significant differences as compared to normal control. ^{c}p<0.001: significant differences as compared to the isoproterenol group. ISO = Isoproterenol (85 mg/kg), HECZ200: hydroalcoholic extract of *Cinnamomum zeylanicum* (200 mg/kg), HECZ400: hydroalcoholic extract of *Cinnamomum zeylanicum* (400 mg/kg), and VIT E = Vitamin E (100 mg/kg).

Table 2. Effects of the hydroalcoholic extract of *Cinnamomum zeylanicum* on hemodynamic and electrocardiographic parameters in Isoproterenol induced myocardial infarction in rats

	Hemodynamic parameters				Electrocardiogram		
	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Mean arterial blood pressure (mmHg)	Heart rate (Beat per minute)	P wave (mV)	QRS complex (mV)	ST wave (mV)
Normal control	124.60 ± 3.03	84.40 ± 3.72	97.80 ± 1.95	376.00 ± 7.28	0.022 ± 0.001	0.545 ± 0.023	0.031 ± 0.001
ISO	86.00 ± 3.03$^{\gamma}$	61.00 ± 2.20$^{\gamma}$	69.33 ± 2.35$^{\gamma}$	409.80 ± 3.73$^{\beta}$	0.019 ± 0.001	0.311 ± 0.025$^{\gamma}$	0.074 ± 0.006$^{\gamma}$
VIT E + ISO	115.20 ± 2.82^{c}	79.80 ± 2.97^{c}	91.60 ± 1.53^{c}	379.00 ± 7.64^{a}	0.023 ± 0.001	0.440 ± 0.026^{a}	0.038 ± 0.002^{c}
HECZ 200 + ISO	114.60 ± 3.20^{c}	80.00 ± 0.70^{c}	91.53 ± 1.42^{c}	378.80 ± 5.28^{a}	0.021 ± 0.001	0.412 ± 0.015$^{\alpha}$	0.046 ± 0.004^{c}
HECZ400 + ISO	117.20 ± 1.88^{c}	77.00 ± 1.73^{b}	90.40 ± 0.79^{c}	375.00 ± 4.72^{b}	0.022 ± 0.001	0.477 ± 0.015^{b}	0.041 ± 0.005^{c}
HECZ 400	99.00 ± 2.02$^{\gamma}$	67.20 ± 2.08$^{\gamma}$	77.80 ± 2.00$^{\gamma}$	364.60 ± 6.08	0.021 ± 0.001	0.477 ± 0.043	0.033 ± 0.002

Each data represents the mean ± SEM. n = 6; $^{\alpha}p$<0.05, $^{\beta}p$<0.01, $^{\gamma}p$<0.001: significant differences as compared to normal control. ^{a}p<0.05 , ^{b}p<0.01, ^{c}p<0.001: significant differences as compared to the isoproterenol group. ISO = Isoproterenol (85 mg/kg), HECZ200: hydroalcoholic extract of *Cinnamomum zeylanicum* (200 mg/kg), HECZ400: hydroalcoholic extract of *Cinnamomum zeylanicum* (400 mg/kg), VIT E = Vitamin E (100 mg/kg).

Table 3. Effects of the hydroalcoholic extract of *Cinnamomum zeylanicum* on some haematological parameters in Isoproterenol induced myocardial infarction in rats

	White blood cell (x 10^3/µL)	**Red blood cell (x 10^6/µL)**	**Platelet (x 10^3/µL)**	**Hemoglobin (g/dL)**	**Hematocrit (%)**	**Mean corpuscular volume (fL)**	**MCH (pg)**	**MCHC (g/dL)**
Normal control	6.35 ± 0.77	7.36 ± 0.28	499.01 ± 7.81	13.37 ± 0.33	37.68 ± 0.97	52.58 ± 3.16	19.26 ± 0.62	37.17 ± 0.70
ISO	9.19 ± 0.59$^{\beta}$	6.68 ± 0.27	469.40 ± 18.84	12.25 ± 0.42	34.45 ± 1.25	53.88 ± 2.01	19.51 ± 0.61	37.62 ± 0.90
VIT E + ISO	6.31 ± 0.48^{b}	7.06 ± 0.32	460.50 ± 21.22	13.18 ± 0.33	35.20 ± 1.60	52.98 ± 2.01	18.76 ± 0.50	37.07 ± 0.87
HECZ 200 + ISO	6.25 ± 0.23^{b}	7.47 ± 0.16	467.20 ± 21.73	13.53 ± 0.25	36.00 ± 1.32	55.72 ± 2.10	18.97 ± 0.61	37.97 ± 1.09
HECZ400 + ISO	6.98 ± 0.19^{b}	7.38 ± 0.15	478.30 ± 25.34	13.13 ± 0.33	35.08 ± 0.89	55.10 ± 2.25	19.02 ± 0.36	35.32 ± 0.25
HECZ 400	6.03 ± 0.37	7.19 ± 0.34	503.01 ± 20.74	13.35 ± 0.42	35.55 ± 1.99	52.58 ± 3.26	18.88 ± 0.42	35.67 ± 0.87

Each data represents the mean ± SEM. n = 6; $^{\beta}p$<0.01 indicate significant differences as compared to normal control. ^{b}p<0.01 indicate significant differences as compared to the isoproterenol group. ISO = Isoproterenol (85 mg/kg), HECZ200: hydroalcoholic extract of *Cinnamomum zeylanicum* (200 mg/kg), HECZ400: hydroalcoholic extract of *Cinnamomum zeylanicum* (400 mg/kg), VIT E= Vitamin E (100 mg/kg), MCH: mean corpuscular hemoglobin concentration, MCHC: mean corpuscular hemoglobin count.

Table 4. Effects of the hydroalcoholic extract of *Cinnamomum zeylanicum* on lipid profile in Isoproterenol induced myocardial infarction in rats

	Total cholesterol (mg/dL)	**High-density lipoproteins (mg/dL)**	**Low-density lipoproteins (mg/dL)**	**triglycerides (mg/dL)**	**Atherogenic index**	**Coronary risk index**
Normal control	65.96 ± 2.52	31.89 ± 1.32	23.52 ± 2.70	43.69 ± 1.32	0.73 ± 0.07	2.08 ± 0.10
ISO	95.83 ± 3.21$^{\gamma}$	22.33 ± 1.16$^{\beta}$	54.40 ± 1.80$^{\gamma}$	75.74 ± 2.61$^{\gamma}$	2.45 ± 0.12$^{\gamma}$	4.31 ± 0.15$^{\gamma}$
VIT E + ISO	73.70 ± 1.75^{c}	35.40 ± 1.69^{c}	28.13 ± 2.36^{c}	43.15 ± 1.09^{c}	0.80 ± 0.08^{c}	2.09 ± 0.01^{c}
HECZ 200 + ISO	71.28 ± 0.90^{c}	39.40 ± 1.87$^{\alpha c}$	21.80 ± 0.68^{c}	45.20 ± 1.75^{c}	0.58 ± 0.04^{c}	1.82 ± 0.09^{c}
HECZ400 + ISO	58.90 ± 1.62^{c}	30.38 ± 1.26^{a}	22.72 ± 0.73^{c}	40.59 ± 0.44^{c}	0.72 ± 0.02^{c}	1.94 ± 0.04^{c}
HECZ 400	54.67 ± 1.27$^{\beta}$	32.82 ± 1.61	17.50 ± 1.09	36.28 ± 1.71	0.54 ± 0.06$^{\beta}$	1.68 ± 0.08

Each data represents the mean ± SEM. n = 6; $^{\alpha}p$<0.05, $^{\beta}p$<0.01, $^{\gamma}p$<0.001: significant differences as compared to normal control. ^{a}p<0.05, ^{b}p<0.01, ^{c}p<0.001: significant differences as compared to the isoproterenol group. ISO = Isoproterenol (85 mg/kg), HECZ200: hydroalcoholic extract of *Cinnamomum zeylanicum* (200 mg/kg), HECZ400: hydroalcoholic extract of *Cinnamomum zeylanicum* (400 mg/kg), VIT E = Vitamin E (100 mg/kg).

Table 5. Effects of the hydroalcoholic extract of *Cinnamomum zeylanicum* on oxidative stress markers and heart proinflammatory cytokines in Isoproterenol induced myocardial infarction in rats

	oxidative stress markers				**heart proinflammatory cytokines**			
	Malondi-aldehyde (µM)	**Superoxide dismutase (U)**	**Catalase (U)**	**Reduced glutathione (nmol)**	**TNF-α (pg/mg of proteins)**	**IL-6 (pg/mg of proteins)**	**IL-1β (pg/mg of proteins)**	**NO (mM)**
Normal control	71.36 ± 0.83	17.68 ± 0.47	10.43 ± 0.86	0.098 ± 0.004	111.00 ± 5.93	41.01 ± 1.79	23.88 ± 1.18	0.124 ± 0.03
ISO	111.00 ± 3.40$^{\gamma}$	9.95 ± 0.73$^{\gamma}$	5.51 ± 0.31$^{\alpha}$	0.045 ± 0.005$^{\beta}$	266.60 ± 18.98$^{\gamma}$	86.90 ± 3.30$^{\gamma}$	50.77 ± 1.27$^{\gamma}$	0.351 ± 0.02$^{\gamma}$
VIT E + ISO	76.08 ± 0.56^{c}	15.72 ± 3.35^{c}	11.06 ± 0.86^{b}	0.088 ± 0.008^{b}	198.60 ± 15.58$^{\gamma b}$	63.22 ± 4.33$^{\gamma c}$	39.71 ± 1.08$^{\gamma c}$	0.195 ± 0.02^{b}
HECZ 200 + ISO	80.16 ± 2.50^{c}	16.75 ± 0.84^{c}	10.15 ± 0.38^{a}	0.092 ± 0.003^{b}	192.00 ± 11.19$^{\beta b}$	56.23 ± 0.84$^{\beta c}$	37.50 ± 1.55$^{\gamma c}$	0.200 ± 0.02^{b}
HECZ400 + ISO	65.79 ± 3.55^{c}	16.63 ± 0.57^{c}	12.96 ± 1.42^{c}	0.100 ± 0.004^{b}	162.80 ± 8.79^{c}	47.38 ± 2.30^{c}	31.32 ± 0.97$^{\alpha c}$	0.172 ± 0.02^{c}
HECZ 400	76.44 ± 0.37	18.73 ± 0.58	11.16 ± 0.82	0.097 ± 0.011	118.80 ± 7.34	41.93 ± 0.91	27.28 ± 2.04	0.136 ± 0.01

Each data represents the mean ± SEM. n = 6; $^{\alpha}p$<0.05, $^{\beta}p$<0.01, and $^{\gamma}p$<0.001 indicate significant differences as compared to normal control. ^{a}p<0.05, ^{b}p<0.01 and ^{c}p<0.001 indicate significant differences as compared to the isoproterenol group. ISO = Isoproterenol (85 mg/kg), HECZ: stem barks hydroalcoholic extract of *Cinnamomum zeylanicum*, and VIT E= Vitamin E (100 mg/kg), TNF-α **=** Tumor necrosis factor-alpha. IL-6 = Interleukin-6, IL-1β = Interleukin-1-beta.

Conclusion

In conclusion, the hydroalcoholic extract of *Cinnamomum zeylanicum* stem bark demonstrated significant cardioprotective effects by preventing oxidative stress, hemodynamic alterations, dyslipidemia, inflammation, and myocardial structural damage in an ISO-induced MI model in rats. These valuable effects are likely due to the antioxidant, hypolipidemic, and anti-inflammatory properties of HECZ, indicating its potential as a healing agent for managing myocardial infarction and related cardiovascular conditions.

Abbreviations

AI: Atherogenic index
ALP: Alkaline phosphatase
ALT: Alanine aminotransferase
AST: Aspartate aminotransferase
BP: Blood pressure
CAT: Catalase
CK-MB: Creatine kinase MB
CRI: Coronary risk index
DBP: Diastolic blood pressure
ECG: Electrocardiogram
EDTA: Ethylene diamine tetra-acetic acid
GSH: Reduced glutathione
HDL-C: High-density lipoproteins cholesterol
HECZ: Hydroalcoholic extract of *Cinnamomum zeylanicum* barks
HR: Heart rate
ISO: Isoproterenol
LDH: Lactate deshydrogenase
LDL-C: High density lipoprotein cholesterol
MABP: Mean arterial blood pressure
MDA: malondialdehyde
MI: Myocardial infarction
NO: Nitric oxide
SBP: Systolic blood pressure
SOD: Superoxide dismutase
TC: Total cholesterol
TG: Total triglyceride
VIT E: Vitamin E or α-Tocopherol

Authors' Contribution

ADA: conceptualization, Investigation, Methodology, Data analysis and processing, Writing – original draft, Writing – review & editing. MFMD: Methodology Writing, Data analysis – review & editing. GNN: Investigation, Methodology, Writing initial manuscript draft. MM: Data analysis and processing, Writing – original draft, Writing – review & editing. FN: Methodology Writing – review & editing, Validation, Supervision TD: Writing – review & editing. All authors reviewed and approved the final version of the manuscript.

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Conflict of interest

The authors declare no conflict of interest

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