Original Article

Histoarchitectural and biochemical investigation of cardiac myocytes in rat model of isoproterenol-induced myocardial infarction with the exploration of boswellic acid

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ABSTRACT

Myocardial infarction is a condition in which loss of myocytes takes place due to prolonged ischemic condition and adrenergic overactivation. Isoproterenol, a synthetic catecholamine and a non-selective β-adrenergic agonist, is often employed in high dose to induce experimental myocardial infarction in order to study cardioprotective anti-infarct effects of pharmacological interventions. Induction of high oxidative stress in the heart is one of key events that could contribute to isoproterenol-induced experimental myocardial infarction. Boswellic acids have potent anti-inflammatory properties, and it has been shown to be beneficial against various inflammatory disorders. In addition to its anti-inflammatory action, boswellic acids have a potent antioxidant potential. However, the protective effect of boswellic acids (250 mg/kg, p.o.) on experimentally induced myocardial infarction has not been investigated. Therefore, the present study has been designed to investigate the effect of boswellic acids against isoproterenol-induced (85 mg/kg, s.c.) myocardial infarction in rats. The present study provides experimental evidence that boswellic acids augmented the myocardial antioxidant enzyme level, preserved histoarchitecture, and improved cardiac performance by changing marker level following isoproterenol administration.

Keywords: Boswellic acid, inflammation, isoproterenol, myocardial infarction, oxidative stress

INTRODUCTION

Ischemic heart disease is a leading cause of mortality worldwide, and its prevalence is incessantly increasing worldwide.[1,2] Myocardial infarction is a condition in which loss of myocytes takes place due to prolonged ischemic condition and adrenergic overactivation.[3,4] Myocardial infarction occurs as a result of coronary artery obstruction, thrombotic occlusion, and coronary spasm-associated myocardial ischemia.[5,6] High oxidative stress and myocardial inflammation play key roles in the pathogenesis of myocardial infarction.[7,8] In addition, increased migration of neutrophils to myocardial ischemic tissue contributes to the pathogenesis of myocardial injury.[9] Acute myocardial infarction is associated with various symptoms such as sudden chest pain radiating to the left arm and shoulder, shortness of breath, anxiety, palpitation, and nausea, vomiting, and sweating.[10]

The chronic and abnormal β-adrenergic receptor overactivation induces cardiac toxicity and myocardial infarction by switching on serial of events. These include activation of Gαs, elevation of cyclic adenosine monophosphate (cAMP) levels, calcium overload, coronary spasm, and reduction in coronary flow.[11-13] Isoproterenol, a synthetic catecholamine and a non-selective β-adrenergic agonist, is often employed in high dose to induce experimental myocardial infarction in order to study cardioprotective anti-infarct effects of pharmacological interventions.[14-16] Isoproterenol-induced myocardial infarction is associated with β-adrenergic sympathetic overactivation. The β-adrenergic Gαs signaling activation results in the elevation of cAMP through adenylyl cyclase activation, leading to phosphorylation

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of L-type calcium channels and elevation of intracellular calcium concentration. This results in ultrastructural changes, alteration of gene transcription, and activation of calcium-dependent endonuclease (DNase I), causing loss of myocytes through apoptosis.[12] It should be noted that elevation in the level of calcium is also a mediator of myocardial necrosis induced by isoproterenol.[17] Induction of high oxidative stress in the heart is one of key events that could contribute to isoproterenol-induced experimental myocardial infarction.[18,19]

In recent years, natural products received much attention as therapeutic agents to treat cardiovascular and metabolic disorders as they are associated with less adverse effects. Boswellic acids are oleo-gum resin obtained mainly from *Boswellia serrata*. The gum resin of boswellic acids comprises β-boswellic acid, 11-keto-β-boswellic acid, and 3-acetyl-11-keto-β-boswellic acid.[20] Boswellic acids have potent anti-inflammatory properties, and it has been shown to be beneficial against various inflammatory disorders, including Crohn's disease, ulcerative colitis, and bronchial asthma.[21-24] In addition to its anti-inflammatory action, boswellic acids have a potent antioxidant potential.[25,26] However, the protective effect of boswellic acids on experimentally induced myocardial infarction has not been investigated. Therefore, the present study has been designed to investigate the effect of boswellic acids against isoproterenol-induced myocardial infarction in rats.

MATERIALS AND METHODS

Experimental animals

The experimental protocol used in the present study was approved by the "Institutional Animal Ethics Committee" in accordance with the guidelines given by "Committee for the Purpose of Control and Supervision of Experiments on Animals." Young Wistar albino rats of either sex weighing 200–250 g average were used in the present study. They were housed in polypropylene cages (47 cm × 34 cm × 20 cm) lined with husk and renewed every 24 h under a 12-h light/dark cycle at around 22°C with 50% humidity. The animals were acclimatized in the institutional animal house and maintained on rat chow (Ashirwad Industries, Mohali, India) and tap water. Rats were given *ad libitum* access to food and water. They were exposed to normal day and night cycles.

EXPERIMENTAL PROTOCOL

As summarized in Table 1, four groups were employed in the present study, and each group comprised six rats. Boswellic acids were suspended in carboxymethyl cellulose (0.5% w/v), and isoproterenol was dissolved in normal saline (NaCl, 0.9% w/v).

In Group I (normal control), rats were maintained on standard food and water, and no treatment shall be given.

In Group II (isoproterenol control), rats were administered isoproterenol (85 mg/kg/day) subcutaneously for the past 2 consecutive days of 30-day experimental protocol.

In Group III (boswellic acids *per se*), normal rats were administered boswellic acids (250 mg/kg/day, p.o.) for 30 days.

In Group IV (boswellic acids pre-treated), rats were pre-treated with boswellic acids (250 mg/kg/day, p.o.) for 30 days. These rats, on the past 2 consecutive days (days 29 and 30), were administered isoproterenol (85 mg/kg/day, s.c.) 1 h after boswellic acid administration.

EXPERIMENTAL AND OBSERVATIONS

Induction of experimental myocardial infarction

Experimental myocardial infarction was induced in rats by administration of isoproterenol hydrochloride (85mg/kg/day, s.c.) for the past 2 consecutive days of 30-day experimental protocol dissolved in freshly prepared normal saline (NaCl, 0.9% w/v).

PARAMETERS EVALUATED

Assessment of myocardial infarction

The isoproterenol-induced myocardial injury was assessed by estimating the release of lactate dehydrogenase (LDH) and creatine kinase-muscle/brain (CK-MB) in the blood serum and measuring the infarct size in the heart. The release of LDH and CK-MB was noted by commercially available kits.

Assessment of myocardial infarct size

The heart was removed from the animal. Both auricles, root of aorta, and right ventricle were excised, and the left ventricle was kept overnight at −4°C. Frozen ventricle was sliced into sections of 2–3 mm in thickness. The slices were incubated in 1% 2,3,5-triphenyltetrazolium chloride (TTC) solution in 0.1 M Tris buffer of pH 7.8 for 20 min at 37°C. The TTC stain reacts with dehydrogenase enzyme in the presence of cofactor NADH to form formazan pigment in viable cells, which are brick red in color. The infarcted cells that have lost dehydrogenase enzyme remain unstained. Thus, the infarcted portion of the myocardium remains unstained while the normal viable myocardium is stained brick red with TTC staining. The infarct size was measured macroscopically using the volume method.[27-29]

Estimation of CK-MB

The amount of released CK-MB in the blood serum was estimated by immunoinhibition method using the commercially available enzymatic kit (Crest Biosystems, Goa, India). It is based on the principle that CK-M fraction of CK-MM and CK-MB in the sample is completely inhibited by CK-M antibody present in the reagent. Then, the activity of CK-B fraction is measured, and the CK-MB activity is expressed in Units per Liter (IU/L). The procedure for CK-MB estimation is described as follows: Briefly, 0.8 mL of enzyme reagent and 0.05 mL of blood serum were taken out in a glass tube and incubated at 37°C for 5 min. Then, 0.2 mL of starter reagent was added to the reaction mixture with thorough mixing. The absorbance was noted against blank, and the initial absorbance was noted after 5 min (A) and thereafter 1 min (B), 2 min (C), and 3 min (D) at 340 nM. The mean change in absorbance per minute was noted, and the CK-MB activity was calculated using the following formula:

CK-MB activity (IU/L) 37°C=ΔA/min×6666

Where, ΔA is [(B-A)+(C-B)+(D-C)]/3.

Estimation of LDH

The amount of released LDH in the blood serum was estimated by ultraviolet-kinetic method using the commercially available enzymatic kit (Crest Biosystems, Goa, India). It is based on the principle that LDH catalyzes the reduction of pyruvate to lactate accompanied by the simultaneous reduction of NADH into NAD. The rate of oxidation of NADH to NAD is proportional to a decrease in absorbance which is proportional to the LDH activity in the sample.

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

The procedure for LDH estimation is described as follows: Briefly, 1 mL of working reagent (mixed contents of bottle of L2 [starter reagent] and bottle L1 [buffer reagent]) was added to 0.05 mL of blood serum in a glass tube with thorough mixing. The absorbance of test was noted against blank exactly after 1 min (A) and thereafter at 2 min (B), 3 min (C), and 4 min (D) at 340 nM. The mean change in absorbance per minute was noted, and LDH activity (expressed in International IU/L) was calculated using the following formula:

LDH activity (IU/L)25°C/30°C=ΔA/min X F

Where, ΔA=[(C-A)+(D-B)]/2XF and F=3333.

Assessment of oxidative stress

The left ventricle was minced and homogenized using potassium chloride (KCl) 1.15%, in a ratio of 1 g of wet myocardial tissue to 10 mL of 1.15% KCl. The tissue homogenate was used to estimate thiobarbituric acid reactive substances (TBARS) and reduced form of glutathione (GSH).

Estimation of myocardial TBARS

The quantitative measurement of TBARS in the rat heart was performed.[30,31] The reaction mixture was prepared by mixing 0.2 mL of tissue homogenate, 0.2 mL of 8.1% sodium dodecyl sulfate, 1.5 mL of 20% acetic acid solution (adjusted to pH 3.5 with NaOH), and 1.5 mL of 0.8% aqueous solution of TBA. The reaction mixture was made up to 4.0 mL with distilled water and then incubated at 95°C for 60 min. After cooling in tap water, 1.0 mL of distilled water and 5.0 mL of the mixture of n-butanol and pyridine (15:1 v/v) were added to reaction mixture and shaken vigorously using vortex shaker. The test tubes were centrifuged at 4000 rpm for 10 min (REMI Cooling Centrifuge, India). The absorbance of developed pink color was measured spectrophotometrically at 532 nM. The standard curve using 1,1,3,3-tetramethoxypropane (1–10 nM) was plotted to calculate the concentration of TBARS [Figure 1], and the results were expressed as nM/g wet weight of myocardial tissue.

Estimation of reduced GSH

The myocardial GSH level was estimated using the methods described by Ellman and Boyne and Ellman.[32,33] The supernatant of heart homogenate of the rat was mixed with 10% w/v trichloroacetic acid in 1:1 ratio and centrifuged at 4°C for 10 min at 5000 rpm. The supernatant (0.5 mL) was mixed with 2 mL of 0.3 M disodium hydrogen phosphate buffer (pH 8.4) and 0.4 mL of distilled water. Then, 0.25 mL of 0.001 M freshly prepared 5,5'-dithiobis(2-nitrobenzoic acid) dissolved in 1% w/v sodium citrate was added to the reaction mixture and then incubated for 10 min. The absorbance of the yellow-colored complex was noted spectrophotometrically at 412 nM. A standard curve was plotted using the reduced form of GSH (0.1–1 µM) [Figure 2], and the results were expressed as µM/g wet weight of myocardial tissue.

Measurement of C-reactive protein (CRP)

The serum CRP, a marker of inflammation, was measured using an immunoassay kit (Immunospec Corporation, CA, USA). This estimation was done from Nalwa Laboratories Pvt. Ltd., Hisar, India. Quantitative measurement of CRP was done in rat serum by turbidimetric immunoassay method. In this method, CRP in the sample binds to specific anti-CRP antibodies, which have been absorbed to latex particles and agglutinations. The agglutination was proportional

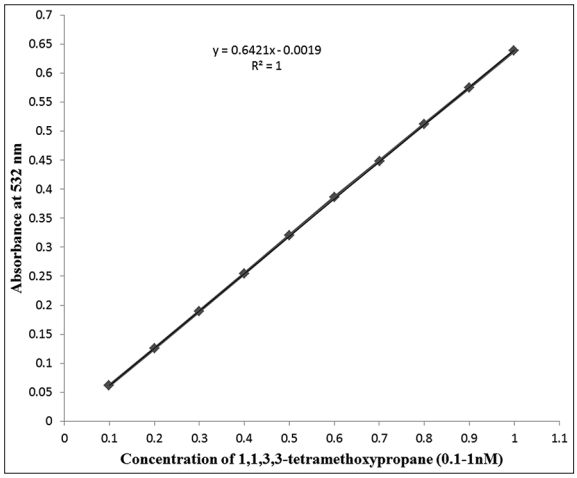

Figure 1: Standard plot of 1,1,3,3-tetra mehoxy propane for estimation of myocardial thiobarbituric acid reactive substances (0.1–1nM)

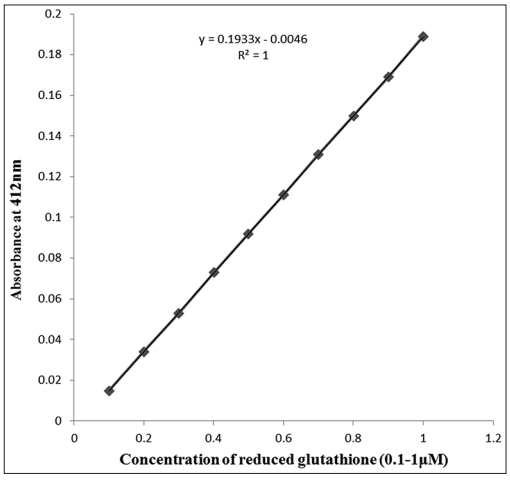

Figure 2: Standard plot of reduced glutathione concentration (0.1–1 µM)

to the quantity of CRP in the sample. The actual concentration was then determined by interpolation from a calibration curve prepared from calibrators of known concentrations.

The CRP concentration was calculated using formula:

$$\text{CRP concentration in mg / L} = \frac{(A_2 - A_1)\ \text{sample}}{(A_2 - A_1)\ \text{calibrator}} \times \text{calibrator concentration}$$

Calibrator concentration=150 mg/L

A1=Initial concentration

A2=Final concentration.

Histopathological assessment

The histological assessment of the myocardium was performed with the help of Haryana Agricultural University, Hisar, Haryana, India. The heart was rapidly dissected and washed immediately with saline and then fixed in 10% buffered neutral formalin solution, and 5-µm thick serial histological sections were obtained from the paraffin blocks and stained with hematoxylin and eosin, after being dehydrated in alcohol (starting from 80% to absolute alcohol) and subsequently cleared with xylene. The histological findings are reported to describe the sites of the lesions; no morphometric evaluations were made in this preliminary study. The photomicrographs were shot using Motic Microscope BA310 (Motic, USA) at ×40 to assess the integrity of myocardium.

Statistical analysis

The results were expressed as mean ± standard deviation. The data obtained from various groups were statistically analyzed using one-way analysis of variance, followed by Tukey's multiple comparison test. $P < 0.001$ was considered statistically significant, and the "*P*" values were of two-tailed.

RESULTS

Administration of boswellic acids *per se* (250 mg/kg/day p.o., 30 days) did not produce any significant effect on various parameters observed in normal rats. Isoproterenol (85 mg/kg/day s.c.) in rats twice at an interval of 24 h on the past 2 consecutive days (days 29 and 30) induces myocardial infarction [Table 1]. Myocardial injury was evaluated by estimating serum parameters such as CK-MB and LDH level, and myocardial infarct size was measured in rat tissue at the end of 4 weeks of experimental protocol. In addition, the serum CRP level was also noted.

Effect of isoproterenol on heart weight/body weight ratio

The effect of boswellic acids treatment on heart weight-to-body weight ratio is depicted in Table 2. There was no significant difference in the body weight between the treated and normal control groups. The heart weight/body weight ratio were increased significantly ($P < 0.001$) in isoproterenol administered rats when compared with normal control rats. Boswellic acid pre-treated rats showed significant ($P < 0.001$) reduction in heart weight/body weight ratio as compared to isoproterenol-treated rats [Figure 3 and Table 2].

Effect of boswellic acids on myocardial infarct size

Increase in myocardial infarct size was seen in isoproterenol-treated group as compared to normal control group. The results obtained were statistically significant in reducing myocardial infarct size. Pre-treatment with boswellic acids (250 mg/kg/day p.o., 4 weeks) significantly attenuated isoproterenol-induced myocardial infarct size changes when compared to normal control group [Figure 4 and Table 2].

Effect of boswellic acids on serum CK-MB and LDH levels

Discernible increase in serum LDH and CK-MB was noted in isoproterenol-induced rats as compared to normal control rats. Pre-treatment with boswellic acids (250 mg/kg/day p.o., 30 days)

Table 1: Summarized experimental protocol employed in the present study

Experiment group	Pharmacological intervention	Dose	Route	Duration
Normal control	–	–	–	30 days
Isoproterenol control	Isoproterenol HCL	85 mg/kg/day	s.c.	Days 29 and 30
Boswellic acids *per se*	Boswellic acids	250 mg/kg/day	p.o.	30 days
Boswellic acids pre-treated	Boswellic acids and Isoproterenol HCL	250 mg/kg/day 85 mg/kg/day	p.o. s.c.	30 days Days 29 and 30

Table: 2 Effect of boswellic acids on various biochemical serum and tissue parameters in rats

Parameters	Normal control	Isoproterenol control	Boswellic acids *per se*	Boswellic acids pre-treated
HW/BW ratio	3.49±0.55	5.50±0.42[a]	2.58±0.21	3.58±0.67[b]
Myocardial infarct size	9.41±1.27	39.83±3.43[a]	7.65±1.25	26.53±3.27[b]
CK-MB	70.3±4.41	245.53±6.65[a]	69.16±6.52	118.6±3.94[b]
LDH	254.2±6.77	594.73±3.65[a]	224.93±6.29	424.2±5.96[b]
TBARS	2.09±0.20	7.99±0.08[a]	2.01±0.15	3.99±0.17[b]
Reduced GSH	30.45±0.76	15.9±1.45[a]	30.06±0.92	25.58±1.20[b]

Values were expressed as mean±SD. [a]$P<0.001$ versus normal control, [b]($P<0.001$) versus isoproterenol control. TBARS: Thiobarbituric acid reactive substances. SD: Standard deviation

restore isoproterenol-induced alterations of serum diagnostic marker enzymes to normal. The results obtained were statically significant in reducing CK-MB [Figure 5] and LDH [Figure 6] levels in isoproterenol-treated rats as compared to normal control rats [Table 2].

Effect of boswellic acids on myocardial oxidative stress

Administration of isoproterenol on the past 2 consecutive days of 30-day experimental protocol (days 29 and 30) showed marked increase in myocardial TBARS when compared to normal rats. In addition, the myocardial concentration of reduced GSH was decreased in isoproterenol-treated rats as compared to normal rats. Beneficial effect of boswellic acids was obtained, and the results were statistically significant showing decrease in myocardial TBARS and restoration of reduced GSH. Treatment with boswellic acids (250 mg/kg/day p.o., 4 weeks) significantly attenuated isoproterenol-induced increase in myocardial TBARS [Figure 7] and decrease in myocardial-reduced GSH level [Figure 8 and Table 2].

Effect of boswellic acids on CRP

Isoproterenol control group significantly showed marked increase in CRP level (3.0 mg/dL), when compared to normal control (1.0 mg/dL). Increased CRP level in isoproterenol-induced rat was significantly attenuated in pre-treated boswellic acid group (1.5 mg/dL) [Table 2].

Effect of boswellic acids on histological changes

Histological changes were evaluated by light microscopy and the structural architecture of normal rats fraying without infarction, where isoproterenol-treated rats showed severe patches of necrotic tissue, inflammatory cells, and edema. In boswellic acids pre-treated group, there were only mild inflammatory cells, edema, and necrotic patches. The treatment effect of boswellic acids restores the structural features of myocardial tissue [Figure 9].

Histopathological analysis

Normal control

The myocardium showed adequate cellularity and normal morphology. Myocytes were healthy, and there was no evidence of myocyte necrosis, nuclear pyknosis, vascular proliferation, macrophage activity, scar formation, or muscle hypertrophy.

Isoproterenol control

The morphological changes occurred in the myocardium that was strongly suggestive of isoproterenol-induced myocardial injury were seen. Large areas of coagulative necrosis were seen with marked congestion of subendocardial blood vessels with a large infarct with margin showing inflammation and hyperemia. Nuclear pyknosis and clumping of cytoplasm were evident throughout areas of necrosis.

Boswellic acids *per se*

The myocardium showed similar pathology as observed in normal control group.

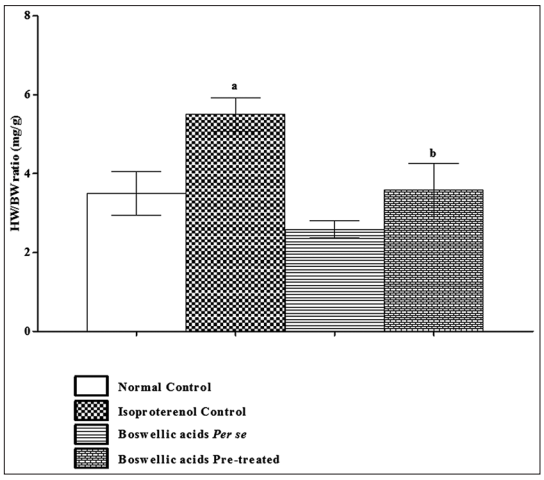

Figure 3: Effect of boswellic acids on heart weight/body weight ratio (mg/g). Values were expressed as mean ± standard deviation. a$P < 0.001$ versus normal control; b($P < 0.001$) versus isoproterenol control

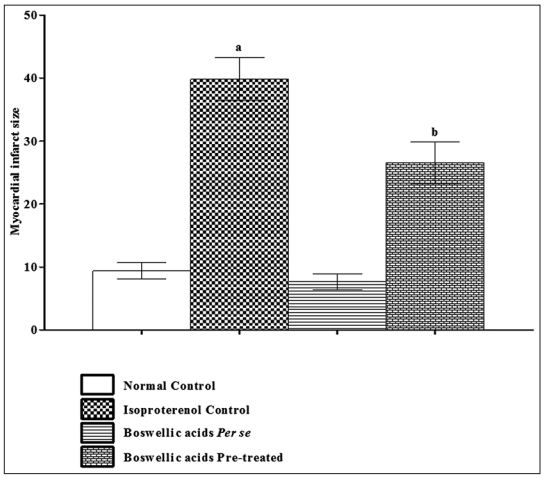

Figure 4: Effect of boswellic acids on myocardial infarct size. Values were expressed as mean ± standard deviation. a$P < 0.001$ versus normal control; b($P < 0.001$) versus isoproterenol control

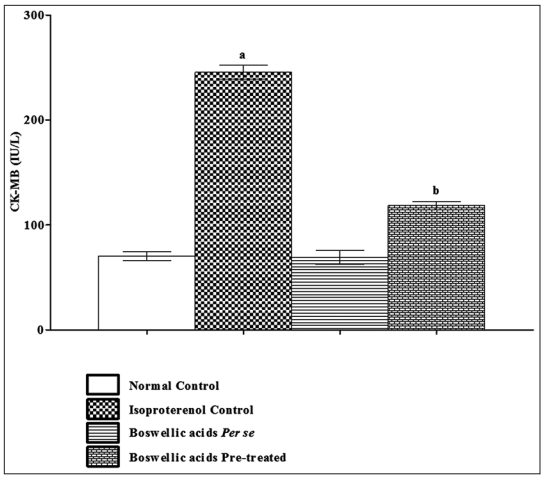

Figure 5: Effect of boswellic acids on myocardial infarct size. Values were expressed as mean ± standard deviation. a$P < 0.001$ versus normal control; b($P < 0.001$) versus isoproterenol control

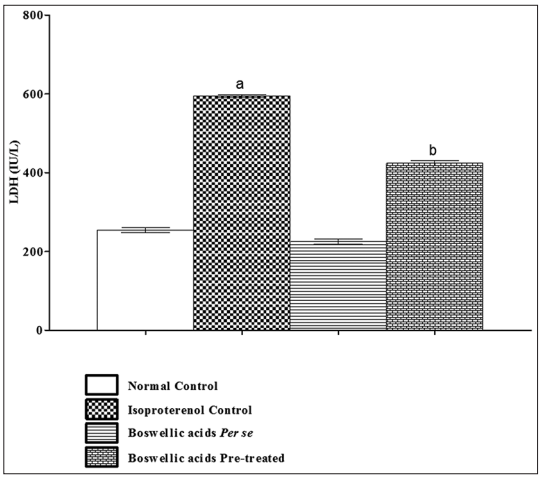

Figure 6: Effect of boswellic acids on serum lactate dehydrogenase (Units per Liter). Values were expressed as mean ± standard deviation. a$P < 0.001$ versus normal control; b($P < 0.001$) versus isoproterenol control

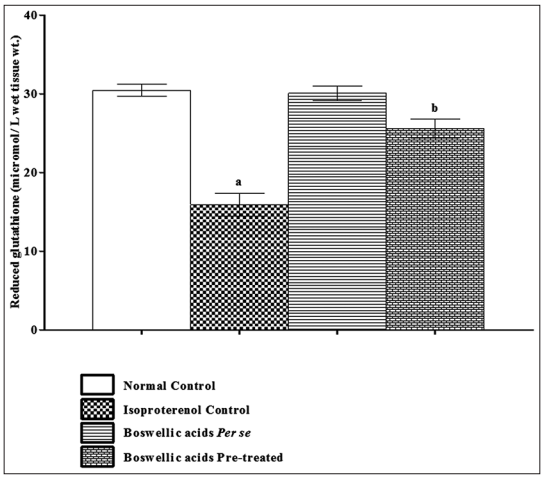

Figure 8: Effect of boswellic acids on myocardial GSH (micromolar/g wet tissue wt). Values were expressed as mean ± standard deviation. a$P < 0.001$ versus normal control; b($P < 0.001$) versus isoproterenol control

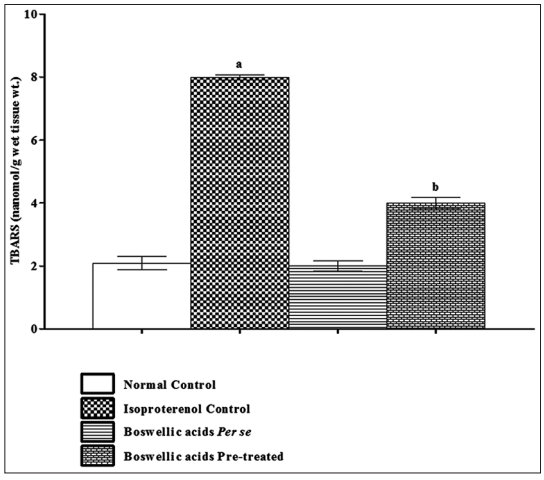

Figure 7: Effect of boswellic acids on myocardial thiobarbituric acid reactive substances (nanomolar/g wet tissue wt). Values were expressed as mean ± standard deviation. a$P < 0.001$ versus normal control; b($P < 0.001$) versus isoproterenol control

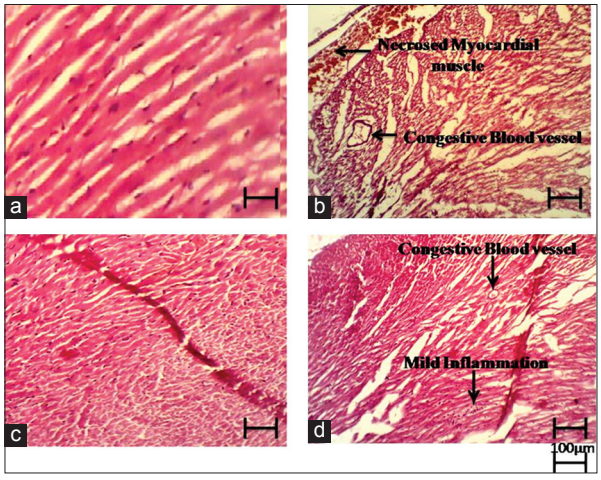

Figure 9: Effect of boswellic acids on histopathological estimation. Figure represents (a) normal control, (b) isoproterenol control, (c) boswellic acids *per se*, and (d) boswellic acids pre-treated

Boswellic acids pre-treated

There was few occurrence of congestion of subendocardial blood vessels with edema of myocardium and mild inflammation. Increased areas of scar formation, vascular proliferation, and macrophage activity were indicative of better healing following myocardial infarction throughout treatment with boswellic acids.

DISCUSSION

The present study demonstrates that the boswellic acids efficiently protect the myocardium against isoproterenol-induced myocardial ischemia. Isoproterenol, a synthetic catecholamine and β-adrenergic agonist, has been found to induce myocardial injury in rats.[34,35] The pathological events caused by isoproterenol in experimental animals mimic the injuries that occur in human myocardium. Zhou *et al.*, 2008, reported that maximum dose of isoproterenol induces subendocardial myocardial ischemia, hypoxia, and necrosis and finally results in fibroblastic hyperplasia with decreased myocardial compliance and inhibition of diastolic and systolic function. These changes closely resemble local myocardial infarction like pathological as well as structural changes observed in human myocardial infarction.[36,37] Further, studies suggest that administration of isoproterenol (85 mg/kg) leads to biochemical and morphological alterations in the heart tissue of experimental animals similar to those observed in human myocardial infarction.[34] Thus, isoproterenol-induced myocardial infarction is widely used model for evaluating cardioprotective drugs and studying myocardial consequences of ischemic disorders.[38] In accordance with the above studies, isoproterenol (85 mg/kg, s.c.) was used in the present study, for induction of myocardial infarction in experimental animals. Treatment with boswellic acids (250 mg/kg, p.o) produced significant prevention from destruction of normal myocardial architecture induced by isoproterenol (85 mg/kg, s.c.) as revealed by evidence of histopathological study.[38] In the normal group, adequate cellularity and normal morphology of myocardium are seen, whereas in isoproterenol-induced group,

large areas of coagulative necrosis, inflammation, and hyperemia were observed indicating myocardial injury. Boswellic acid-treated group showed few occurrence of congestion of subendocardial blood vessels and mild inflammation, which were indicative of better healing following myocardial infarction. These findings suggest that boswellic acids have protective action against isoproterenol-induced myocardial infarction. Boswellic acids have a potent antioxidant potential.[25,26] In the present study, the degree of oxidative stress in the experimental rats was assessed by estimating TBARS and reduced GSH. An increase in the levels of TBARS and decrease in reduced GSH level in the heart tissue of isoproterenol-induced rats were observed. Boswellic acid treatment significantly reverses the levels of markers which cause oxidative stress proving its antioxidant potential. It has been also reported that CK-MB is present in the higher proportion and concentration in the injured myocardium and also referenced as early marker of myocardial infarction. Moreover, LDH levels get elevated when there are tissue inflammation and necrosis. Numerous researchers have also reported the elevated levels of CK-MB and LDH in isoproterenol-induced myocardial infarction.[39-41] In accordance with the above studies, the present results also showed increase in CK-MB and LDH levels in isoproterenol group. Treatment with boswellic acids significantly decreases the levels of CK-MB and LDH when compared to isoproterenol control animals. Further, isoproterenol-injected rats showed a significant rise in serum CRP level indicative marker of inflammation. CRP has been used as a sensitive predictor of acute cardiovascular events when compared with other widely used biomarkers.[42] The observational studies have reported that serum CRP concentrations are inversely associated with dietary intake of fruits, vegetables, and tea, which are rich in polyphenolic antioxidants.[39,43] Treatment with boswellic acids significantly reduced the elevated CRP levels suggesting its potent antioxidant and anti-inflammatory activity. Isoproterenol treatment significantly increased the heart weight-to-body weight ratio showing isoproterenol-mediated cardiac hypertrophy in rats.[39,44] There was a significant difference in the heart weight-to-body weight ratio between normal control and isoproterenol control groups. Boswellic acid treatment significantly reduced the heart weight to body weight and attributes its cardioprotective effect in the present results.

It is concluded from the present study that boswellic acids improve necrotic damage, restore antioxidant defense, reduce oxidative stress and inflammation induced by isoproterenol, and prove its cardioprotective action against myocardial infarction.

CONCLUSION

Boswellic acids significantly prevent the damages induced by isoproterenol on histopathological and biochemical changes in rat model of myocardial infarction. Boswellic acids ameliorate the cardiotoxic effect of isoproterenol in rat heart. The present study provides experimental evidence that boswellic acids augmented the myocardial antioxidant enzyme level, preserved histoarchitecture, and improved cardiac performance by changing marker level following isoproterenol administration. These findings suggest the beneficial cardioprotective effects of boswellic acids on rat heart against experimental myocardial infarction, and it should further be explored against other cardiac complications.

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