Research article

# Protective effect of sesamol against myocardial infarction caused by isoproterenol in Wistar rats

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This study was designed to investigate the cardioprotective effect of sesamol on isoproterenol (ISO)-induced myocardial infarction in adult male albino Wistar rats. The heart damage induced by ISO was indicated by elevated levels of the marker enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatine kinase (CK), creatine kinase-MB (CK-MB) and the levels of troponin T and I in the plasma. In addition, lipid peroxidative markers such as thiobarbituric acid reactive substances (TBARS), conjugated dienes (CD) and lipid hydroperoxides (LHP) significantly increased in the plasma and heart. Activities of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione-*S*-transferase (GST) and glutathione reductase (GR) significantly decreased in the heart and (non-enzymic antioxidants) vitamin C, vitamin E and reduced glutathione (GSH)) levels significantly decreased in the plasma and heart in ISO-rats. Histopathological observations correlated with the biochemical parameters. Administration of sesamol at different doses 50, 100 and 200 mg/kg body weight intraperitoneally for 7 days prevented the above changes and improved towards normality; the 50 mg dose was more effective than the other two doses.

**Keywords:** isoproterenol, myocardial infarction, sesamol, antioxidants

## Introduction

Cardiovascular diseases (CVDs) are the major health problem of highly developed as well as developing countries of the world.[1] Myocardial infarction (MI) is one of the main causes of death from CVD. MI is the acute condition of necrosis of the myocardium that occurs as a result of imbalance between coronary blood supply and myocardial demand. Experimental induction of MI by isoproterenol in animals is a well-established model to study the protective role of various cardioprotective agents. Isoproterenol (ISO), a synthetic β-adrenoceptor agonist, has been found to induce myocardial injury in rat as a result of a disturbance in the physiological balance between production of free radicals and the antioxidant defence system.[2] Under normal physiological conditions, formation of free radials is limited by the endogenous antioxidant defence system. In ischaemic heart disease, the production of free radicals is increased at a rate that overwhelms the capacity of the endogenous antioxidant defence system for detoxification, thereby resulting in free radical mediated oxidative damage.[3] Myocardial cell protection and prevention of cell ischaemia/necrosis have been therapeutic targets for a long time. New therapies are needed to treat myocardial ischaemia because current treatment has only a limited impact on survival and annual costs. Currently, there is increasing realization that plant products can

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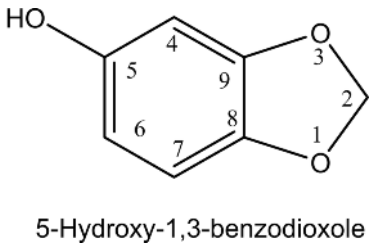


5-Hydroxy-1,3-benzodioxole

**Figure 1 Structure of sesamol**

influence the course of heart disease and its treatment. Recently, phytophenols have been attracting much attention as active constituents in functional foods and food supplements. Some phytophenols, especially polyphenolic compounds, show a very potent antioxidant activity. The activity is closely linked to various beneficial actions including anti-aging, prevention of cancer and cardiovascular disease.[4]

Sesamol (5-hydroxy-1,3-benzodioxole) is a phenolic derivative with a methylenedioxy group and, like vitamin E, is known to be an antioxidant contained mainly in processed sesame oil.[5] Sesamol is formed from the decomposition of sesamolin (present in sesame oil with sesamin) during the processing of sesame oil. Sesame oil, derived from the plant species *Sesamum indicum* L. has been found to contain considerable amounts (up to 15%) of the sesame legans, sesamin and sesamolin. Sesamol is a unique dietary phenolic compound as it is stable in the physiological pH range, soluble in both aqueous and lipid phases and stable at high cooking temperatures. Sesamol has been reported to act as a metabolic regulator and to possess antioxidant,[6] anti-aging,[7] antimutagenic,[8] antihepatotoxic,[9] chemopreventive[10] and anticarcinogenic activity and inhibits atherosclerosis.[11] No study has been carried out on the cardioprotective effect of sesamol on ISO-induced MI. Hence, in the present study, we attempted to investigate the anti-ischaemic effect of sesamol in ISO-induced myocardial ischaemia. The structure of sesamol is given in Figure 1.

## Materials and methods

### *Animals*

Male albino rats of Wistar strain with a body weight ranging from 180–200 g were procured from the Central Animal House, Department of Experimental Medicine, Rajah Muthiah Medical College and Hospital, Annamalai University, and maintained in an air-conditioned room (25 ± 1ºC) with a 12-h light/12-h dark cycle. Feed and water were provided *ad libitum*. All experimental studies were conducted in the Department of Biochemistry, Faculty of Science, Annamalai University. The experimental study protocol was approved by the Animal Ethics Committee of Rajah Muthiah Medical College and Hospital (Reg No.160/1999/CPCSEA, Pro. No. 579), Annamalainagar.

### *Chemicals*

Isoproterenol hydrochloride and sesamol were purchased from Sigma Chemical Co. (St Louis, MO, USA). The purity of sesamol is ~99% (TLC). All other chemicals and reagents used were of analytical grade from E. Merck (Mumbai, India).

### *Experimental induction of myocardial ischaemia*

Myocardial ischaemia was induced by subcutaneous (sc) injection of isoproterenol hydrochloride (ISO, 85 mg/kg body weight), dissolved in physiological saline, for two consecutive days in the morning at 10.00 am.[12]

### *Experimental design*

The rats were randomly divided in to six groups of eight rats each. Sesamol dissolved in saline (0.9% NaCl) was administered intraperitoneally once in a day in the morning for 7 days.

| | |
|---|---|
| Group I | Control (0.9% saline only) |
| Group II | Control + sesamol (200 mg/kg body weight) |
| Group III | ISO control (85 mg/kg body weight, sc, twice at an interval of 24 h on 1st and 2nd day) |
| Group IV | ISO + sesamol (50 mg/kg body weight) |
| Group V | ISO + sesamol (100 mg/kg body weight) |
| Group VI | ISO + sesamol (200 mg/kg body weight) |

The total experimental duration was 9 days. After treatment, the animals were anaesthetized between 8:00–9:00 am using ketamine (24 mg/kg body weight by intramuscular injection), and sacrificed by cervical dislocation. The blood was collected in a heparinized centrifuge tube, centrifuged at 2000 rpm for 10 min and the plasma was separated. Serum was separated by centrifugation at 2000 rpm for 10 min. The serum samples were used for cardiac marker assay. The heart tissue was sliced into pieces and homogenised in appropriate buffer in cold conditions (pH 7.0) to give 20% homogenate (w/v). The homogenate was centrifuged at 1000 rpm for 10 min at 0ºC in a precooled centrifuge. The supernatant was separated

and used for various biochemical estimations. For histopathological study, three rats from each group were perfused with cold physiological saline, followed by formalin (10% formaldehyde). The heart tissues were excised immediately and fixed in 10% formalin. Then, the tissues were dehydrated by treatment with a series of different concentration of ethanol and embedded in paraffin wax. sections (3-5 μm thick) were cut using a microtome and stained with haematoxylin and eosin. The specimens were evaluated with light microscopy. All histopathological changes were examined by a pathologist.

*Biochemical estimations*

The activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were assayed by the method of Reitman and Frankel.[13] Lactate dehydrogenase (LDH), creatine kinase (CK) and creatine kinase–MB (CK-MB) activities were determined by the methods of King[14] and Okinaka *et al.*,[15] respectively, using commercially available kits. Plasma cardiac troponin T and I (cTnT and cTnI) were quantitatively measured by means of a highly specific enzyme immunoassay using commercially available kits.[16,17] The level of thiobarbituric acid reactive substances (TBARS), lipid hydroperoxides (LHPs), and conjugated dienes were estimated by the methods of Niehaus and Samuelson,[18] Jiang *et al.*,[19] and Rao and Recknagel,[20] respectively. The levels of vitamin C, vitamin E, and reduced glutathione (GSH) were estimated by the method of Roe and Kuether,[21] Baker *et al.*,[22] and Ellman,[23] respectively. The protein content was determined by the method of Lowry *et al.*[24] Enzymic antioxidants, superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), glutathione-S-transferase (GST) and glutathione reductase (GR) activities were assayed by the methods of Kakkar *et al.*,[25] Sinha,[26] Rotruck *et al.*,[27] Habig *et al.*,[28] and Pinto and Bartley,[29] respectively.

*Statistical analysis*

Statistical analyses were performed by one-way analysis of variance (ANOVA) and groups were compared by Duncan's Multiple Range Test (DMRT) using SPSS Software Package v.10.0. Results were expressed as mean ± SD for six rats in each group. A value of $P \leq 0.05$ was considered to be statistically significant.

## Results

The activities of serum AST, ALT, LDH, CK, CK-MB and the level of troponin T and I in the plasma of control and experimental rats are given in Table 1. Increased activities of AST, ALT, LDH, CK, CKMB and increased level of troponin T and I were observed in the ISO-induced rats. Treatment with sesamol at doses of 50, 100 and 200 mg/kg body weight lowered the above parameters significantly. The 50-mg dose improved the activities of AST, ALT, LDH, CK, CK-MB and the level of troponin T and I to near normal levels.

The levels of TBARS, LHP and CD in the plasma and heart are summarized in Table 2. The levels of TBARS, LHP and CD were significantly elevated in the ISO administered rats and treatment with sesamol significantly decreased the levels of TBARS, LHP and CD.

The activities of SOD, CAT, GPx, GST and GR are given in Table 3. SOD, CAT, GPx, GST and GR activities significantly decreased in ISO-induced rats and treatment with sesamol significantly restored the activities.

**Table 1 Effect of sesamol on serum AST, ALT, LDH, CK, CK-MB and plasma troponins T and I in control and isoproterenol rats**

| Groups | AST (IU/l) | ALT (IU/l) | LDH (IU/l) | CK (IU/l) | CK-MB (IU/l) | Troponin T (ng/ml) | Troponin I (ng/ml) |
|---|---|---|---|---|---|---|---|
| Control | 66.60 ± 6.10$^{a}$ | 18.83 ± 1.48$^{a}$ | 201.42 ± 15.85$^{a}$ | 144.80 ± 12.04$^{a}$ | 95.43 ± 7.33$^{a}$ | 0.59 ± 0.05$^{a}$ | 0.38 ± 0.02$^{a}$ |
| Control + sesamol (200 mg/kg BW) | 93.42 ± 8.10$^{b}$ | 39.67 ± 2.94$^{b}$ | 242.03 ± 12.11$^{b}$ | 187.45 ± 11.54$^{b}$ | 134.77 ± 10.14$^{b}$ | 0.98 ± 0.08$^{b}$ | 0.60 ± 0.04$^{b}$ |
| ISO (85 mg/kg BW) | 115.69 ± 9.26$^{c}$ | 44.42 ± 4.70$^{c}$ | 277.21 ± 14.99$^{c}$ | 217.01 ± 18.91$^{c}$ | 155.52 ± 10.07$^{c}$ | 1.20 ± 0.11$^{c}$ | 0.66 ± 0.05$^{c}$ |
| ISO + sesamol (50 mg/kg BW) | 71.30 ± 5.22$^{a}$ | 22.61 ± 1.54$^{a}$ | 210.75 ± 10.91$^{d,a}$ | 155.97 ± 7.67$^{a}$ | 104.13 ± 7.95$^{a}$ | 0.66 ± 0.05$^{d,a}$ | 0.42 ± 0.04$^{a}$ |
| ISO + sesamol (100 mg/kg BW) | 82.72 ± 6.77$^{d}$ | 34.13 ± 3.03$^{d}$ | 222.62 ± 8.75$^{d}$ | 171.14 ± 7.86$^{d}$ | 121.57 ± 9.14$^{d}$ | 0.74 ± 0.07$^{d}$ | 0.48 ± 0.04$^{d}$ |
| ISO + sesamol (200 mg/kg BW) | 104.39 ± 9.77$^{e}$ | 45.46 ± 4.48$^{e}$ | 258.95 ± 9.86$^{e}$ | 202.67 ± 10.78$^{e}$ | 145.03 ± 6.44$^{e}$ | 0.84 ± 0.07$^{e}$ | 0.55 ± 0.05$^{c}$ |

Values are given as mean ± SD from six rats in each group.

$^{a–f}$Values sharing a common superscript do not differ significantly at $P < 0.05$ (DMRT).

**Table 2 Effect of sesamol on TBARS, LHP and CD in the plasma and heart of control and isoproterenol-treated rats**

| Groups | TBARS | | LHP | | CD | |
|---|---|---|---|---|---|---|
| | Plasma (mmol/dl) | Heart (mmol/100 g wet tissue) | Plasma (mmol/dl) | Heart (mmol/100 g wet tissue) | Plasma (mmol/dl) | Heart (mmol/100 g wet tissue) |
| Control | 0.14 ± 0.01[a] | 0.44 ± 0.03[a] | 9.25 ± 0.59[a] | 62.07 ± 5.80[a] | 0.69 ± 0.06[a] | 37.28 ± 3.26[a] |
| Control + sesamol (200 mg/kg BW) | 0.26 ± 0.01[b] | 0.71 ± 0.04[b] | 12.52 ± 0.92[b] | 84.11 ± 8.45[b] | 0.99 ± 0.09[b] | 57.45 ± 3.63[b] |
| ISO (85 mg/kg BW) | 0.36 ± 0.02[c] | 0.87 ± 0.07[c] | 14.91 ± 1.33[c] | 102.91 ± 7.68[c] | 1.25 ± 0.11[c] | 70.90 ± 6.56[c] |
| ISO + sesamol (50 mg/kg BW) | 0.16 ± 0.01[a] | 0.49 ± 0.03[a] | 10.48 ± 0.46[d] | 68.15 ± 5.47[d,a] | 0.76 ± 0.04[a] | 46.52 ± 2.93[d] |
| ISO + sesamol (100 mg/kg BW) | 0.21 ± 0.02[d] | 0.64 ± 0.04[d] | 11.57 ± 0.98[e] | 74.75 ± 6.07[d] | 0.86 ± 0.06[d] | 51.40 ± 5.01[d] |
| ISO + sesamol (200 mg/kg BW) | 0.31 ± 0.02[e] | 0.79 ± 0.06[e] | 14.59 ± 0.73[f] | 94.96 ± 5.73[e] | 1.10 ± 0.07[e] | 63.47 ± 4.38[e] |

Values are given as mean ± SD from six rats in each group.
[a–f]Values sharing a common superscript do not differ significantly at $P < 0.05$ (DMRT).

**Table 3 Effect of sesamol on vitamin C, vitamin E, and GSH in the plasma and heart of control and isoproterenol-treated rats**

| Groups | Vitamin C | | Vitamin E | | GSH | |
|---|---|---|---|---|---|---|
| | Plasma (mg/dl) | Heart (μg/mg protein) | Plasma (mg/dl) | Heart (μg/mg protein) | Plasma (mg/dl) | Heart (μg/mg protein) |
| Control | 2.68 ± 0.19[a] | 0.59 ± 0.02[a] | 1.89 ± 0.10[a] | 3.04 ± 0.19[a] | 39.78 ± 2.55[a] | 8.70 ± 0.68[a] |
| Control + sesamol (200 mg/kg BW) | 1.78 ± 0.14[b] | 0.48 ± 0.04[b] | 1.50 ± 0.09[b] | 2.38 ± 0.08[b] | 29.04 ± 2.39[b] | 6.43 ± 0.57[b] |
| ISO (85 mg/kg BW) | 1.31 ± 0.12[c] | 0.33 ± 0.03[c] | 1.19 ± 0.09[c] | 1.96 ± 0.10[c] | 19.05 ± 1.02[c] | 4.98 ± 0.40[c] |
| ISO + sesamol (50 mg/kg BW) | 2.44 ± 0.17[d] | 0.56 ± 0.02[a,d] | 1.80 ± 0.15[a] | 2.83 ± 0.19[d] | 36.95 ± 3.39[a,d] | 8.10 ± 0.63[a] |
| ISO + sesamol (100 mg/kg BW) | 2.06 ± 0.22[e] | 0.53 ± 0.04[d] | 1.64 ± 0.12[d] | 2.59 ± 0.18[e] | 34.41 ± 2.26[d] | 7.31 ± 0.51[d] |
| ISO + sesamol (200 mg/kg BW) | 1.53 ± 0.12[f] | 0.40 ± 0.02[e] | 1.34 ± 0.07[e] | 2.16 ± 0.20[f] | 23.67 ± 2.22[e] | 5.63 ± 0.28[e] |

Values are given as mean ± SD from six rats in each group.
[a–f]Values sharing a common superscript do not differ significantly at $P < 0.05$ (DMRT).

**Table 4 Effect of sesamol on the activities of SOD, CAT, GPx, GR and GST in the heart of control and isoproterenol-treated rats**

| Groups | SOD ($U^1$/mg protein) | Catalase ($U^2$/mg protein) | GPx ($U^3$/mg protein) | GST ($U^4$/mg protein) | GR ($U^5$/mg protein) |
|---|---|---|---|---|---|
| Control | 7.98 ± 0.59[a] | 56.58 ± 3.81[a] | 6.99 ± 0.47[a] | 6.06 ± 0.31[a] | 6.19 ± 0.33[a] |
| Control + sesamol (200 mg/kg BW) | 6.53 ± 0.58[b] | 49.07 ± 3.91[b] | 5.30 ± 0.33[b] | 4.57 ± 0.32[b] | 4.64 ± 0.40[b] |
| ISO control (85 mg/kg BW) | 5.11 ± 0.46[c] | 32.23 ± 4.35[c] | 4.17 ± 0.32[c] | 3.46 ± 0.37[c] | 3.73 ± 0.30[c] |
| ISO + sesamol (50 mg/kg BW) | 7.87 ± 0.42[a] | 54.76 ± 4.37[a] | 6.56 ± 0.51[a] | 5.64 ± 0.42[d] | 5.73 ± 0.33[d] |
| ISO + sesamol (100 mg/kg BW) | 7.19 ± 0.67[d] | 42.54 ± 3.98[d] | 5.86 ± 0.44[d] | 5.06 ± 0.25[e] | 5.09 ± 0.37[e] |
| ISO + sesamol (200 mg/kg BW) | 5.88 ± 0.48[c] | 36.83 ± 2.60[c] | 4.73 ± 0.38[c] | 4.08 ± 0.30[f] | 4.11 ± 0.26[f] |

Values are given as mean ± SD from six rats in each group.
[a–f]Values sharing a common superscript do not differ significantly at $P < 0.05$ (DMRT).
$U^1$ Enzyme concentration required to inhibit the chromogen produced by 50% in 1 min under standard condition.
$U^2$ μmole of hydrogen peroxide decomposed/min.
$U^3$ μmole of GSH utilized/min.
$U^4$ μg of CDNB conjugate formed/min.
$U^5$ μg of reduced glutathione formed/min.

Changes in the levels of non-enzymic antioxidants such as vitamin C, vitamin E and GSH in the plasma and heart are shown in Table 4. ISO caused a decrease in the levels of vitamin C, vitamin E and GSH and administration of sesamol significantly increased the levels and the best effect was observed with the 50-mg dose.

Histopathological changes of the heart in control and ISO-induced rats are shown in Figure 2. ISO-induced rats showed a rupture of muscle fibres and mononuclear infiltration and treatment with sesamol at 50 mg/kg body weight brought these changes towards near normality. Normal rats treated with sesamol at higher doses showed the collection of mononuclear cells among hypertrophic cardiac muscle bundles.

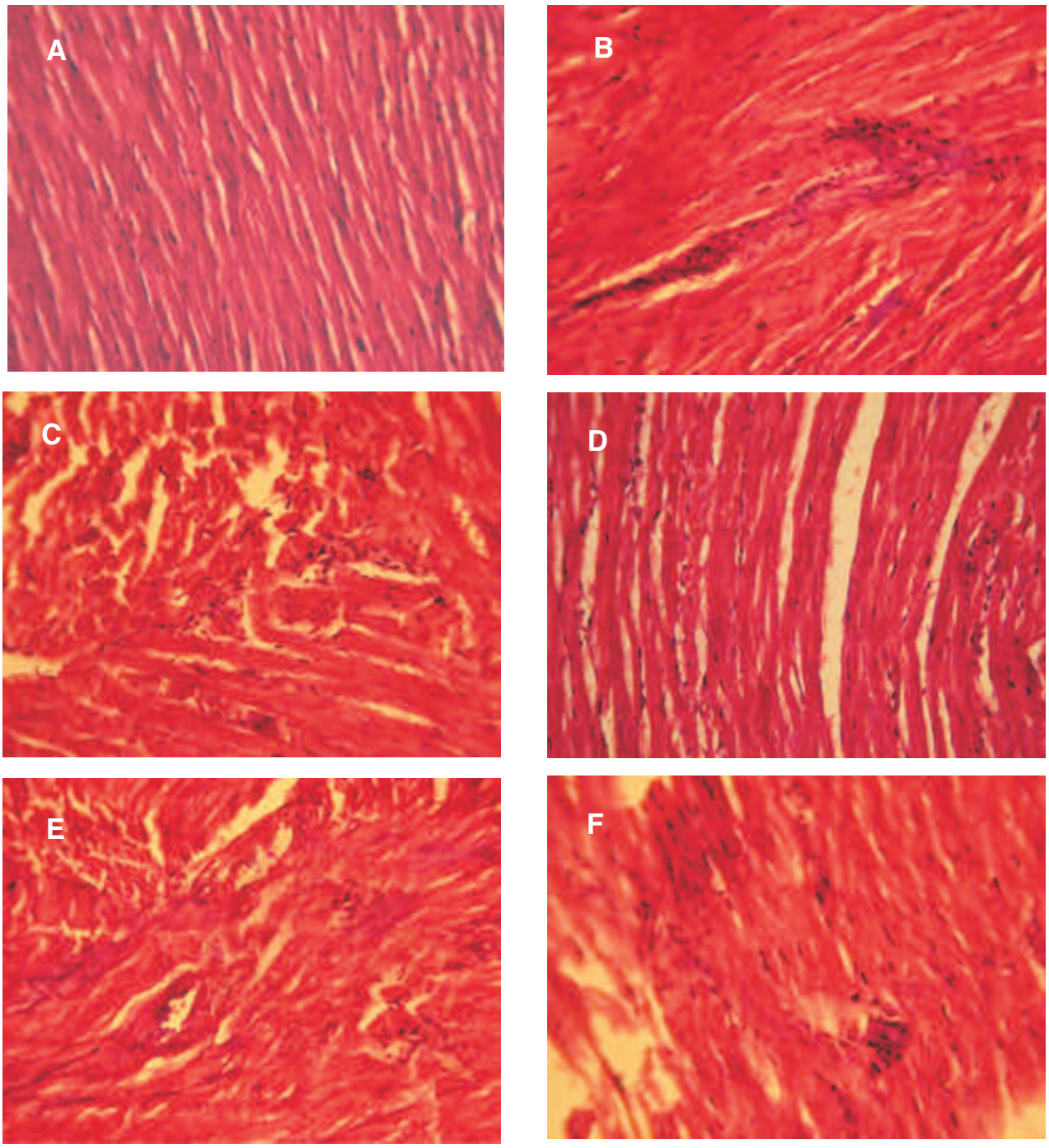


**Figure 2** **Histopathological changes of cardiac muscle (haemotoxylin and eosin 400×). (A) Normal cardiac muscle bundles. (B) Normal rats with sesamol – collection of mononuclear cells among hypertrophic cardiac muscle bundles. (C) MI control – rupture of muscle fibres and mononuclear infiltration. (D) MI with 50 mg sesamol reduced the rupture of muscle fibres and mononuclear infiltration. (E) MI with 200 mg sesamol – hypertropic with mild reduction of rupture of cardiac muscle fibres. (F) MI with 100 mg sesamol – focal collection of mononuclear cells and fibrosis**

## Discussion

Isoproterenol, a potent synthetic catecholamine, when administered to animals at high doses produces 'infarct-like' lesions in the heart, which are similar to those found in myocardial infarction (MI) in humans.[30] Myocardium contains an abundant concentration of marker enzymes (AST, ALT, CK, CK-MB and LDH) of MI and, once metabolically damaged, it releases its contents into the extracellular fluid. Cardiac troponin T (cTnT) and troponin I (cTnI) are currently the most sensitive and specific cardiac markers of MI. The initial rise in cardiac

troponins (cTnT and cTnI) after myocardial infarction occurs at about the same time as CK and CK-MB, but this rise continues for longer than for most of the enzymes, possibly because of later release of insoluble troponin from the infarcted muscle. In this study, increased activities of AST, ALT, CK, CK-MB and LDH and the levels of troponin T (cTnT) and troponin I (cTnI) were observed in the plasma of ISO-induced rats, which is consistent with earlier report.[31] Hsu *et al*.[32] reported that sesamol decreases the serum levels of aspartate aminotransferase and alanine aminotransferase in iron-intoxicated mice. In our study, administration of sesamol at doses of 50, 100 and 200 mg/kg body weight significantly lowered the activities of marker enzymes and the levels of troponins in ISO-induced rats.

The increased free radicals produced can react with polyunsaturated fatty acids in cell membrane leading to lipid peroxidation, which will, in turn, result in elevated free radical production.[33] Senthil *et al*.[34] reported that the concentrations of TBARS, HP and CD were significantly increased in the plasma and heart of ISO-induced experimental rats. The increased concentration of lipid peroxidative markers suggests an increase in oxygen free radicals, either by increased production or decreased destruction. In our study, ISO-administered rats also showed an increase in the levels of lipid peroxidation products (TBARS, CD and LHP) in the plasma and heart. Previously, Hsu *et al*.[32] reported that sesamol significantly reduced the hydroxyl radical, superoxide anion generation and lipid peroxidation in mice injected with Fe-NTA (ferric-nitrilotriacetate). Sesamol treatment of the ISO-induced rat decreased the lipid peroxidation level. The antilipid peroxidative effect of sesamol in ISO-administered rats might be due to diminished formation of hydroxyl radical and superoxide anion.

High concentrations of isoproterenol administration have been reported to induce severe oxidative stress and result in necrotic lesions in the myocardium of rats.[2] The increased production of reactive oxygen species and/or depletion of the antioxidants in the defence system may contribute to oxidative stress and affect the pathogenesis of myocardial infarction. Free radical scavenging enzymes such as SOD, CAT, GPx, GST and GR are the first line of cellular defence against oxidative stress. The equilibrium between these enzymes is a significant process for the effective removal of oxygen stress in intracellular organelles. SOD reacts with the superoxide radicals to form $H_2O_2$. CAT and GPx are involved in the detoxification of $H_2O_2$. CAT is an important enzyme in preventing the formation of hydroxyl radicals.[35] GPx also has a vital role in quenching $H_2O_2$ and other peroxides which otherwise lead to production of hydroxyl and peroxyl radicals. GR is another important enzyme for the maintenance of intracellular concentrations of reduced glutathione (GSH). GSH together with GST, GPx, GR, and the CAT-SOD couple efficiently scavenge free radical species such as $H_2O_2$, superoxide anions and alkoxyl radicals. As a substrate for antioxidant enzymes GPx and glutathione-S-transferase (GST), GSH protects cellular constituents from the damaging effects of ROS and peroxides formed during metabolism. It has been well documented that ISO causes increased oxidative stress in rat heart as evidenced by reduction in myocardial SOD, GPx,[36] CAT, GST[37] and GR[38] activities, also observed in our study. After administration of sesamol, increased activities of these enzymes have been observed and similar results were obtained for GPx and GST in radiation-induced cytotoxicity after treatment with sesamol.[35]

The second line of defence consists of the non-enzymic scavengers such as vitamin E, vitamin C and GSH, which scavenge free radicals escaping from decomposition by the antioxidant enzymes. In the aqueous environment, ascorbic acid has numerous antioxidant properties, including the ability to regenerate α-tocopherol by reducing α-tocopheroxyl radicals present on the surface of membranes.[39] Vitamin C acts on exposure to ROS and prevents binding of toxic free radicals to nucleic acid or proteins both *in vivo* and *in vitro*.[40] The decreased level of vitamin C in ISO-induced rats may be due to the increased utilization as an antioxidant defence against increased ROS or a decrease in glutathione level, since glutathione is required for the recycling of ascorbic acid. Vitamin E is the most effective lipid soluble antioxidant in biological systems. It inhibits lipid peroxidation by scavenging lipid peroxyl radicals to yield lipid hydroperoxide and α-tocopheroxyl radical. The decrease in vitamin E, in ISO-administered rats, might be due to the increased utilization in scavenging the oxyradicals generated or due to decreased vitamin C level because there is a well-established interaction between vitamin E and vitamin C. The decrease in vitamin E level is in line with other observations in which plasma and heart lipid peroxides are increased during myocardial ischaemia. In sesamol-treated rats, the level of vitamin E increased, which might be due to decreased the lipid peroxidation. GSH is one of the most abundant non-enzymic antioxidant biomolecules present in the body. In our study, the levels of GSH decreased in ISO-induced myocardial necrosis. The decreased level of GSH could result in the decreased removal of free radicals and these radicals bring about a number of reactions which are harmful to the

myocardium. An increased level of GSH was observed in rats treated with sesamol, which quenches the free radical formation during myocardial necrosis. It was thought that this antioxidant property is due to the phenolic hydroxyl group present in the sesamol. We found that a 200-mg dose of sesamol is toxic to the animals and abnormal physiological activity like 'seizures' was observed for 20 min; thereafter, it returned to normality with 25% death.

Histopathological examination of myocardium of ISO-treated rats revealed rupture of muscle fibres and mononuclear infiltration. In this regard, 50 mg of sesamol-treated rats with ISO administration attenuated the pathological features induced by ISO as evident from the histopathological examinations, indicating their cardioprotective effect.

## Conclusions

This study has demonstrated that sesamol at a dose of 50 mg/kg body weight had more cardioprotective effect then the other two doses (100 mg and 200 mg), which is evidenced by lowered cardiac marker enzymes, lipid peroxidation products and increased antioxidants in the ISO-induced rats is greatest in those treated with 50 mg sesamol.

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