Cardioprotective and Antioxidant Potential of Scilla hyacinthina

K. Sakthivel, S. Palani, R. Selvaraj, D. Venkadesan, H. Sivasankari and B. Senthil Kumar

Department of Biotechnology, Anna Bioresearch Foundation, Arunai Engineering College, Tiruvannamalai, India

Department of Zoology, Tiruvalluvar University, Vellore, Tamilnadu, India

**Abstract:** The present study were designed to scientifically evaluate the cardioprotective potential of ethanolic extract of *Scilla hyacinthina* (Family: Hyacinthinae), a medicinal herb, on Doxorubicin (DOX) induced myocardial infarction (MI) in albino rats. DOX is one of the most effective chemotherapeutic drugs in cancer, however, its incidence of cardiotoxicity compromises its therapeutic index. DOX-induced heart failure is thought to be caused by reduction/oxidation cycling of DOX to generate oxidative stress and cardiomyocyte cell death. A Doxorubicin dose of 20 mg kg⁻¹ was selected for the present study as this dose offered significant alteration in biochemical parameters and moderate necrosis in heart. Effect of SHA oral treatment for 14 days at two doses (250 and 500 mg kg⁻¹ b.wt) was evaluated against DOX-induced cardiac necrosis. Significant myocardial necrosis, depletion of endogenous antioxidants and biochemical parameters were observed in DOX-treated animals when compared with the normal animals. The pretreatment with SHA to DOX-induced rats significantly prevented the altered biochemical variation such as marker enzymes (SGPT, SGOT, CPK and LDH), lipid profile (LDL, VLDL, TGs, HDL and Total cholesterol) and antioxidant parameters (SOD, GSH, CAT, GSH-Px, MDA and GR) to near normal status. Serum urea, uric acid and alkaline phosphate, which increased on DOX administration, registered near normal values on pretreatment with SHA. Histology of pretreated with SHA to DOX-induced heart showed a significant recovery from cell damage. The present findings have demonstrated that the cardioprotective effects of SHA in DOX-induced oxidative damage may be due to an augmentation of the endogenous antioxidants and inhibition of lipid peroxidation of membrane.

**Key words:** Cardioprotective, antioxidant, Scilla hyacinthina, doxorubicin, myocardial infarction

**INTRODUCTION**

Myocardial infarction (MI) is an acute condition of necrosis of the myocardium that occurs as a result of imbalance between coronary blood supply and myocardial demand (De Bono and Bocn, 1992). An increased risk of MI is associated with high levels of serum total cholesterol (Grundy, 1986) and Low Density Lipoprotein (LDL) (Brown and Goldstein, 1986) and decreased levels of High Density Lipoprotein (HDL) (Castelli et al., 1986). Oxidative stress produced by free radicals or Reactive Oxygen Species (ROS) as evidenced by marked increase in production of lipid peroxidative products and transient inhibition of endogenous antioxidant defense such as superoxide dismutase (SOD catalase (CAT) and reduced glutathione (GSH) has been shown to underlie myocardial damage during MI (Loper et al., 1991; Padmanabhan and Prince, 2006; Zhou et al., 2008). Minimizing myocardial necrosis and improving heart function have been proved to be effective strategies to reduce the morbidity and mortality from myocardial infarction (Kloner and Rezkalla, 2004). Accordingly, antioxidants may decrease cellular injury and apoptosis through a radical-scavenging mechanism (Angioloni et al., 2007). Therapeutic intervention via suppression of free radical generation and/or augment endogenous antioxidant enzymes may attenuate myocardial dysfunction. An anthraquinone anticancer drug, doxorubicin is effective against malignancies such as leukemias, lymphomas and several solid tumors. However, dose-dependent cardiotoxic effects limit its practical therapeutic use. Thus DOX is reported to increase oxygen free radical activity (Lee et al., 1991) as well as induces the peroxidation of unsaturated lipids within the membranes (Myers et al., 1977).

Although modern drugs are effective in preventing cardiovascular disorders, their use is often limited because of their side effects (Rajadurai and Prince, 2005). Herbal drugs are prescribed widely, even when their biologically active compounds are unknown, because of their effectiveness, lesser side effects and relatively low cost (Kumar et al., 2008). Now-a-days, the usage

**Corresponding Author:** K. Sakthivel, Department of Biotechnology, Anna Bioresearch Foundation, Arunai Engineering College, Tiruvannamalai, Tamilnadu, India
of herbal drugs is gaining greater acceptance from the medical and public profession due to their positive contribution and influence on health and quality of life. So, search for indigenous cardioprotective herbal drugs is still continuing as part of scientific research.

*Scilla* is a genus of bulb-forming perennial herbs in the Hyacinthaceae family, a preparation of powdered bulbs extracted in ethanol, is an ingredient in cough medicines and cardiac surgery. The leaf and fruits of *Scilla hyacinthina* (Roth.) Macbr., are reported to possess antiasthmatic, diuretic, expectorant and cardio stimulant activity (Sudhersan and Padmanabhan, 1993). Extensive phytochemical investigations carried out on SHA revealed the presence of many chemical constituents including palmitic and linoleic acid such as n- Hexadecanoic acid, 9,12-Octadecadienoic acid (Z,Z)- and oleic acid, which are considered significant for Hypcholesterolemic property (Kurian et al., 2010; Lee et al., 2005; Mohamed et al., 2009). All these factors and lack of scientific data on the cardiac activities led to the investigation of the cardioprotective potential of SHA, ethanolic extract in rat models. Therefore, the present study was designed to investigate the effects of SHA on DOX-induced myocardial necrosis in rats.

**MATERIALS AND METHODS**

**Kurian**

**Preparation of Scilla hyacinthina extract:** Leaves of *Scilla hyacinthina* (Roth.) Macbr. Was collected and identified and authenticated (AECBT 10/2010) by a Botanist, Dr. C. Madhavachetty, Tirupathi university, Tirupathi, India. Materials were cleaned with water and dried in the shade until a constant weight was obtained. It was extracted with 95% ethanol in a Soxhlet extractor. Extracts were concentrated; the percentage yield for ethanol extract was 7.9% and for pharmacological studies, since the ethanol extract was not soluble in water, it is suspended in 5% gum acacia.

**GC-MS analyses of ethanol extract of SHA for the identification of chemical composition:** The identification of chemical composition of ethanol extract of SHA was performed using a GC-MS spectrograph (Agilent 6890/ Hewlett-Packard 5975) fitted with Electron Impact (EI) mode. The ethanol extract (2.0 mL) of SHA was injected with a Hamilton syringe to the GC-MS manually for total ion chromatographic analysis in split mode. In quantitative analysis, Selected Ion Monitoring (SIM) mode was employed during the GC MS analysis. SIM plot of the ion current resulting from very small mass range with only compounds of the selected mass were detected and plotted.

**Induction of experimental myocardial infarction:** Doxorubicin was dissolved in sterile double distilled water and injected subcutaneously to rats (20 mg kg⁻¹) after last dose of the extract to induce experimental MI (Singh et al., 2008).

**Experimental animals:** Studies were carried out using Wistar albino rats (150-200 g), obtained from Indian Veterinary Preventive Medicine (IVPM), Ranipet, Tamilnadu, India. The animals were housed in polycarbonate cages (38, 23, 10 cm) and maintained under standard laboratory conditions (temperature 25-20°C) with dark/light cycle (12/12 h). The animals were fed with standard pellet diet (supplied by poultry research station, Nandhanam, India) and fresh water ad libitum. All the animals were acclimatized to lab conditions for a week before commencement of the experiment. All the procedures described were reviewed and approved by the University Animal’s Ethical Committee.

**Experimental procedure:**

- **Group 1:** (Normal). Saline (0.75 ml/animal), orally for 14 days
- **Group 2:** (Drug control). Saline (0.75 mL animal⁻¹)+ DOX 20 mg kg⁻¹, single intraperitoneal injection after 14th day
- **Group 3:** (Extract control). SHA (500 mg kg⁻¹), orally for 14 days
- **Group 4:** (Extract control). SHA (500 mg kg⁻¹), orally for 14 days+ DOX (20 mg kg⁻¹) single intraperitoneal injection after 14th day
- **Group 5:** (Extract control). SHA (500 mg kg⁻¹), orally for 14 days+ DOX (20 mg kg⁻¹) single intraperitoneal injection after 14th day

**Isolation of working heart preparation:** The animals were anesthetized with chloroform after 72 h of DOX administration and then heart was punctured with sterile syringe and blood was stored with EDTA which is an anticoagulant agent and was excised out. Cardiac muscle from lower third of the ventricle was visualized under light microscope and the remaining heart tissue was snap frozen in liquid nitrogen.

**Histopathological studies:** Since it has been ascertained that DOX-induced myocardial lesions are focal and uniformly scattered throughout the whole organ, isolated trial preparation were used instead of the whole heart owing to the greater stability of response and reproducibility of the results. The hearts were removed, washed immediately with saline and then fixed in 10%
buffered formalin. The hearts stored in 10% buffered formalin were embedded in paraffin, sections cut at 5 mm and stained with hematoxylin and eosin. These sections were then examined under a light microscope for histoarchitectural changes.

**Biochemical analysis**: Blood sample were collected into tubes pre-coated with EDTA by vein puncture at baseline and post intervention. Samples were prepared by centrifuging for 10 min 3000 x g at 4°C. Plasma, puffy coat and red blood cell sub-fractions were collected and stored at -80°C until further analysis. The serum used for the assay of marker enzymes as well as urea, uric acid, was estimated by the methods of Caraway (1963) and respectively. The activities of Serum Glutamate-pyrurate Transaminase (SGPT) and Serum Glutamate Oxaloacetate Transaminase (SGOT) in serum were determined spectrophotometrically by the method of Mohun and Cook (1957). The Lactate Dehydrogenase (LDH) and Creatine Phosphokinase (CPK) were determined by the method of King (1965) and by the method of Okinaka el at. (1961), respectively. The levels of total cholesterol and triglycerides (TGs) were estimated by the methods of Zlatkis et al. (1953) and Foster and Dunn (1973). Serum High Density Lipoprotein (HDL) was determined according to the method of Wilson and Spiker (1973). Serum low density lipoproteins (LDL) and very low density lipoproteins (VLDL) were calculated as VLDL=total cholesterol-LDL. The heart was dissected, immediately washed in ice-cold saline and a homogenate was prepared in 0.1 M Tris-HCl buffer (pH 7.4). The homogenate was centrifuged and the supernatant was used for the assay of antioxidant parameters. MDA content was measured according to an earlier method Zhang (1992). Superoxide dismutase (SOD) activity was determined according to Rai et al. (2006). CAT activity was determined from the rate of decomposition of H₂O₂ according to Bergmeyer et al. (1974). Glutathione peroxidase (GSH-Px) activity was determined by measuring the decrease in GSH content after incubating the sample in the presence of H₂O₂ and NaI according to Hafeman et al. (1974). GSH reductase activity was assayed according to Carlberg and Mannervik (1975) and Mohandas et al. (1984). GR activity was determined according to the method described by Staal et al. (1969).

**Statistical analysis**: The obtained results were analyzed for statistical significance using one way ANOVA followed by Dunnett test statistical software for comparison with control group and acetaminophen treated group. The p<0.05 was considered as significant.

**RESULTS**

**Phytochemical analysis**: The ethanol extract of SHA was a complex mixture of many constituents and compounds were identified in this plant by GC-MS (Table 1). Phytoconstituents such as n-Hexadecanoic acid (13.97%), 9.12-Octadecadienoic acid (Z,Z)-(5.36%), Oleic Acid (12.63%), 2-Pyrrolizine, 5-hydroxy-3-methyl-5-trifluoromethyl-1-(3,4-dimethylphenoxacyltyl)-(21.01%), 4H-1,3-Dithiin, 2,2,6-trimethyl-1-(2,2,6-trimethyl-1H,1,3-dithiin-4-ylidene)-(16.35%), 2-Thiophenecarboxaldehyde, 5-ethyl-2-(2,4-dimethoxyphenyl) hydrazone (11.09%), 4H-1-Benzopyran-4-one, 5,7-dihydroxy-2-(3,4,5-trimethoxymethyl)- (8.46%), Octadecenoic acid (4.64%), 1-Octanol, 3,7-dimethyl-(0.87%), 1-Heptanol, 2-propyl-(0.20%), 2-Isopropyl-5-methyl-1-heptanol (0.95%), 1-

<table>
<thead>
<tr>
<th>RT</th>
<th>Name of the compound</th>
<th>Molecular formula</th>
<th>MW</th>
<th>Peak area (%)</th>
<th>Compound nature</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.60</td>
<td>Glycerin</td>
<td>C₃H₆O₃</td>
<td>92</td>
<td>1.74</td>
<td>Alcohol</td>
</tr>
<tr>
<td>4.78</td>
<td>1-Octanol, 3,7-dimethyl-[Synonym: Dihydrocitronellol]</td>
<td>C₁₀H₁₇O₂</td>
<td>158</td>
<td>0.87</td>
<td>Terpine alcohol</td>
</tr>
<tr>
<td>6.93</td>
<td>Decane, 2,3,5,8-tetramethyl</td>
<td>C₁₃H₂₆O</td>
<td>198</td>
<td>0.44</td>
<td>Alkane</td>
</tr>
<tr>
<td>7.47</td>
<td>1-Heptanol, 2-propyl</td>
<td>C₁₁H₂₂O</td>
<td>158</td>
<td>0.20</td>
<td>Alcohol</td>
</tr>
<tr>
<td>7.88</td>
<td>2-Isopropyl-5-methyl-1-heptanol</td>
<td>C₁₂H₂₀O</td>
<td>172</td>
<td>0.95</td>
<td>Alcohol</td>
</tr>
<tr>
<td>9.04</td>
<td>Diphenyinethane</td>
<td>C₁₂H₁₄O</td>
<td>168</td>
<td>0.09</td>
<td>Aromatic compound</td>
</tr>
<tr>
<td>9.80</td>
<td>1-Octanol, 2-butyal</td>
<td>C₁₀H₁₄O</td>
<td>186</td>
<td>0.28</td>
<td>Alcohol compound</td>
</tr>
<tr>
<td>16.19</td>
<td>n-Hexadecanoic acid</td>
<td>C₁₆H₃₂O₆</td>
<td>256</td>
<td>13.97</td>
<td>Palmitic acid</td>
</tr>
<tr>
<td>16.49</td>
<td>Hexadecanoic acid, ethyl ester</td>
<td>C₁₆H₃₂O₂</td>
<td>284</td>
<td>0.49</td>
<td>Estor compound</td>
</tr>
<tr>
<td>18.45</td>
<td>Phytol</td>
<td>C₁₀H₁₈O</td>
<td>286</td>
<td>0.30</td>
<td>Diterpene</td>
</tr>
<tr>
<td>18.78</td>
<td>9,12-Octadecadienoic acid (Z,Z)-</td>
<td>C₁₆H₂₆O₂</td>
<td>280</td>
<td>5.36</td>
<td>Limonoid acid</td>
</tr>
<tr>
<td>18.86</td>
<td>Oleic Acid</td>
<td>C₁₇H₃₃O₂</td>
<td>282</td>
<td>12.65</td>
<td>Oleic acid</td>
</tr>
<tr>
<td>19.18</td>
<td>Octadecanoic acid</td>
<td>C₁₆H₃₂O₂</td>
<td>284</td>
<td>4.64</td>
<td>Storacid</td>
</tr>
<tr>
<td>23.25</td>
<td>4H-1-Benzopyran-4-one, 5,7-dihydroxy-2-(3,4,5-trimethoxymethyl)-</td>
<td>C₁₆H₂₆O₆</td>
<td>344</td>
<td>8.46</td>
<td>Flavonoid compound</td>
</tr>
<tr>
<td>24.72</td>
<td>1,2-Benzene dicarboxylic acid, diosoyl ester</td>
<td>C₁₂H₁₆O₂</td>
<td>300</td>
<td>1.12</td>
<td>Plasticizer compound</td>
</tr>
<tr>
<td>30.63</td>
<td>2-Thiophenecarboxaldehyde, 5-ethyl-2-(2,4-dimethoxyphenyl)</td>
<td>C₁₆H₁₈O₄S</td>
<td>316</td>
<td>11.09</td>
<td>Sulfur compound</td>
</tr>
<tr>
<td>31.40</td>
<td>4H-1,3-Dithiin, 2,2,6-trimethyl-1-(2,2,6-trimethyl-1H,1,3-dithiin-4-ylidene)</td>
<td>C₁₆H₁₄S₄</td>
<td>316</td>
<td>16.35</td>
<td>Sulfur compound</td>
</tr>
<tr>
<td>32.39</td>
<td>2-Pyrrolizine, 5-hydroxy-3-methyl-5-trifluoromethyl-1-(3,4-dimethylphenoxacyltyl)-</td>
<td>C₁₆H₂₆F₅N₂O₇</td>
<td>330</td>
<td>21.01</td>
<td>Alkaloid</td>
</tr>
</tbody>
</table>
Fig. 1: GCMS analysis of ethanolic SHA leaf extract

Octanol, 2-butyl- (0.28), Hexadecanoic acid, ethyl ester (0.49%) and Phytoph (0.30%), were identified in the ethanolic extract of SHA by relating to the corresponding peak area through coupled GC-MS (Fig. 1).

**Fig. 2:** Effect of ethanolic extract SHA on Urea (mg dL⁻¹), Uric acid (mg dL⁻¹), GR (nmol of NADPH oxidized/min/100 mg protein) and alkaline phosphate (mg dL⁻¹) in DOX intoxicated rats, Values are Mean±S.D (n = 6) **p<0.01, ***p<0.05, respectively.

**Fig. 3:** Effect of ethanolic extract SHA on SGOT (IU L⁻¹) and SGPT (IU L⁻¹) in DOX intoxicated rats, Values are Mean±S.D (n = 6) **Significant at p<0.05 and 0.01, respectively

**Effect of SHA extract on serum markers during DOX induced cardiotoxicity:** The serum markers indicating myocardial injury, LDH, CPK, SGPT and SGOT were significantly (p<0.01) elevated in the DOX-only treated group compared with normal and SHA-only treated group (Fig. 3 and 4). Pretreatment with SHA (250 and 500 mg kg⁻¹ b.wt) group (group 4 and 5) significantly reduced their levels as compared with DOX-only treated group (group 2).

**Effect of SHA extract on serum markers during DOX induced cardiotoxicity:** The serum markers indicating myocardial injury, LDH, CPK, SGPT and SGOT were significantly (p<0.01) elevated in the DOX-only treated group compared with normal and SHA-only treated group (Fig. 3 and 4). Pretreatment with SHA (250 and 500 mg kg⁻¹ b.wt) group (group 4 and 5) significantly reduced their levels as compared with DOX-only treated group (group 2).
Effect of SHA extract on antioxidant parameters: DOX-induced rats (group 2) had exhibited a significant (p<0.01) decrease in activities of CAT, SOD, GSH-Px and GSH level as compared to normal rats (group 1). Although SHA (250 and 500 mg kg day\(^{-1}\)) dose dependently counteracted the deleterious effect of DOX by increasing the content of these antioxidants, significance could be achieved with 500 mg kg day\(^{-1}\) dose of SHA only (p<0.01) (Fig. 7). Administration of SHA alone (500 mg day\(^{-1}\)) (group 3) did not show significant changes in antioxidants as compared to normal rats. There is significant reduce in the GR during the SHA administration to the DOX induced heart when compared to the normal (group 1).

Cardiac lipid peroxidation assessed by MDA production did not rise in the pretreated rats after DOX administration when compared with DOX - induced rats (Fig. 7).

Histopathological findings: Cardiotoxicity induced by DOX (group 2) was further assessed using H and E stain. The heart from normal group (group 1) showed a regular cell distribution and normal myocardium morphology (Fig. 8). Histology of the rat from DOX-induced animals (group 2) revealed the cytoplasmic vacuole formation and myofibrillar loss, which is typical finding in DOX induced cardiomyopathy. Heart myocardial lesions were significantly reduced in animals that received SHA treatment (group 4 and 5).
DISCUSSION

Cardiotoxicity caused by treatment with Doxorubicin can be life-threatening and may occur even years after completion of therapy (Kapusta et al., 2000). The current study entails the cardioprotective potential of the ethanolic extract of SHA against DOX-induced cardiotoxicity. Serum CPK, SGPT, SGOT and LDH are well known markers of myocardial infarction. When myocardial cells are damaged or destroyed due to deficient oxygen supply or glucose, the cardiac membrane becomes permeable or may rupture which results in leakage of enzymes. These enzymes enter into the blood stream thus increasing their concentration in the serum (Mathew et al., 1985). Activities of these enzymes in serum decreased in SHA pretreated DOX induced group probably due to the protective effect of SHA on myocardium, which had reduced the extent of myocardial damage induced by DOX and thereby restricting the leakage of these enzymes from myocardium. It is widely accepted that oxygen-free radicals generated during Doxorubicin redox cycling are responsible for the damage that doxorubicin causes to the heart (Julicher et al., 1985; Singal and Iliskovic, 1998; Van Acker et al., 1997; Venditti et al., 1998). Oxygen radical generation affects the heart because doxorubicin and its toxic metabolite
doxorubicin accumulate in cardiac tissue that has low antioxidant levels (De Jong et al., 1991).

Cardioprotective activity of SHA is supported by increased myocardial antioxidant enzyme activity and decreased extent of lipid peroxidation. The most abundant ROS generated in living cells are superoxide anion and its derivatives, particularly highly reactive and damaging hydroxyl radical, which induces peroxidation of cell membrane lipids (Hennani and Parihar, 1998). Lipid peroxidation is known to cause cellular damage and is primarily responsible for ROS-induced organ damage (Halliwell and Gutteridge, 1989). Our studies have shown that DOX-induced MI considerable increased in lipid peroxidation, which was significantly prevented by SHA pretreatment.

Redox cycling of DOX generates superoxide free radicals (Hrdina et al., 2000) due to conversion of quinone to semi-quinone moiety, whereas SOD enzyme dismutase this free radical to hydrogen peroxide. In this respect, any increase in SOD activity of the organ appears to be beneficial in the event of increased free-radical generation. Our studies showed that the activity of SOD was significantly decreased in DOX-treated animals and the pretreatment with SHA reversed the SOD activity in dose-dependent manner. However, it has been reported that a rise in SOD activity, without a concomitant rise in the activity of catalase/GSH might be detrimental (Herman, 1991). This is due to the fact that SOD generates hydrogen peroxide as a metabolite, which is cytotoxic and needs to be scavenged by catalase/GSH. Thus a simultaneous increase in catalase/GSH activity is essential for an overall beneficial effect of increase in SOD activity (Mukherjee et al., 2003). Inhibition of DOX-induced oxidative stress and tissue injury might be due to an increase in GSH, myocardial SOD and catalase activities, following the pretreatment of SHA. The observed increase in catalase activity in DOX-treated animals supports the above hypothesis that this increase is possibly required to overcome excessive oxidative stress (Li and Singal, 2000).

Uric acid is considered to be a risk factor in the development of MI (Upston et al., 1999). We observed significance increase in the level of plasma uric acid DOX induced rats which could be due to increased free radical production by DOX. In hypoxic tissue, ATP depletion occurs which leads to accumulation of hypoxanthine when tissues are disturbed, the enzyme Xanthine Dehydrogenase is converted to Xanthine Oxidase by the oxidation of essential SH groups. Xanthine Oxidase catalyzes the conversion of Hypoxanthine to Xanthine, Uric acid to super oxide (Weir et al., 2003). This could be one of the reasons for the elevated levels of plasma uric acid in DOX induced rats.

GSH levels were also lowered significantly in DOX-treated animals, while pretreatment with SHA showed significant increase in GSH levels in DOX-treated animals at doses of 250 and 500 mg kg⁻¹ in rats. Catalase activity was increased after DOX treatment and pretreatment of SHA further increased its activity significantly at 250 and 500 mg kg⁻¹ dose levels. The increase in catalase activity in DOX-treated animals could be indicative of enhanced oxidative stress due to a adaptive myocardial mechanism.

Myocardial infarction (MI) is also associated with altered lipid metabolism. The increased concentration of cholesterol could be due to a decrease in HDL, since HDL is known to be involved in the transport of cholesterol from tissues to the liver for its catabolism (Mathew et al., 1981). In this context, we have observed decreased levels of HDL in DOX-treated rats. The observed increase in TGs might be due to a decrease in the activity of lipoprotein lipase, resulting in decreased uptake of TGs from the circulation (Kumari et al., 1990) and also reported that the decreased levels of phospholipids in DOX-treated rats might be due to the enhanced membrane degradation. Pretreatment with SHA decreases the concentration of total cholesterol, TGs, VLDL and increases the concentration of HDL in heart of DOX-induced rats. These changes in lipid levels might be due to enhanced lipid biosynthesis by cardiac cyclic adenosine monophosphate (Paritha and Devi, 1997). Studies have shown that high levels of LDL cholesterol have a positive correlation with MI, whereas high levels of HDL cholesterol have a negative correlation with MI (Buring et al., 1992). These findings indicate the promising role of SHA as a cardioprotective agent against DOX-induced cardiotoxicity.

CONCLUSION

The present study shows that the administration of ethanolic extract of SHA has cardioprotective potential against Dox-induced cardiotoxicity. It provides experimental evidence that SHA augmented the myocardial antioxidant enzymes level, preserved histoarchitecture and improved cardiac performance following DOX administration. This cardioprotective activity of SHA might be due to the synergetic effect of chemical compounds present in them making them good sources for the production of a cardioprotective herbal...
medicine. The identification of molecules with cardioprotective potential from this ethanolic extract of SHA may provide new directions for identification of cardioprotectives, which could be given concomitantly during Dox treatment.

REFERENCES


