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RESEARCH ARTICLE

EFFECT OF SINAPIC ACID ON HEART RATE, ENZYMATIC ANTIOXIDANTS, CARDIAC AND AORTIC LIPIDS IN L-NAME INDUCED HYPERTENSIVE RATS

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ABSTRACT

The present study was designed to evaluate the antihypertensive and antihyperlipidemic effect of sinapic acid (SA), a phenolic acid against N^{ω}-nitro-L arginine methyl ester hydrochloride (L-NAME) induced hypertension in male Wistar rats. Hypertension was induced by oral administration of L-NAME (40 mg/kg body weight (bw)) in drinking water for 4 weeks. Rats were treated with SA (10, 20 and 40 mg/kg bw) for four weeks. L-NAME treated rats showed significant increase in heart rate and water intake. The activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) were decreased in erythrocytes of L-NAME rats. L-NAME rats showed significant increase in the levels of lipids such as total cholesterol (TC), triglycerides (TG), free fatty acids (FFA) and significant decrease in the level of phospholipids (PL) in heart and aorta. Histopathological examination of heart and aortic tissues confirmed the pathological changes induced by hypertension. Above pathological changes were considerably restored with the treatment of sinapic acid. These results suggest that SA acts as an antihypertensive and antihyperlipidemic agent against L-NAME induced hypertension.

INTRODUCTION

Hypertension is the most common cardiovascular disorder both in developed and in developing countries and has emerged as one of the major causes of mortality and morbidity worldwide (Mattila and Kumpulainen, 2002). It affects more than 600 million people and results in 13% of total deaths globally, and it is estimated that there will be 29% of the world's adult with hypertension by 2025 (Mittal and Singh, 2010). Hypertension frequently occurs in conjunction with metabolic disturbances and in particular with dyslipidemia (Chapman and Sposito, 2008). In humans, hypertension and hyperlipidemia are frequent causes of cardiovascular disease (CVD) and major risk factors for atherosclerosis; the presence of both conditions accelerates atherosclerosis (Kwon *et al*., 1998). Nitric oxide (NO) synthesis and release by endothelial cells play an important vascular relaxation effect, contributing to the modulation of vascular tone (Mori *et al*., 2006). NO is one of the smallest biologically active molecules that are produced from L-arginine by nitric oxide synthase (NOS) (de-Belder and Radomski, 1994). The chronic administration of nitric oxide synthase inhibitors provides an animal experimental model of hypertension (Silva-Herdade and Saldanha, 2011). Chronic inhibition of NO synthesis by the administration of L-NAME (Nω-nitro-L arginine methyl ester hydrochloride) inhibits NOS activity, leading to hypertension, atherosclerosis and cardiac remodeling (Sanada *et al*., 2003). Recent evidence indicates that oxidative stress as the main mechanism is responsible for cardiovascular complications such as alteration in lipid metabolism (Palmieri *et al*., 2006). Oxidative stress, originally described as an altered balance between the production of free radicals and antioxidant defenses, is an important phenomenon in different physiological and pathological processes (Chang and Wu, 2006).

Lifestyle and dietary habits may affect blood pressure and cardiovascular risk factors (Zhou *et al*., 2006). In recent years, the prevention of cardiovascular diseases has been associated with ingestion of fresh fruits, vegetables or plants rich in natural antioxidants (Retelny *et al*., 2008). Phenolic compounds form a substantial part of plant foods. Most of these phenolic compounds are antioxidants *in vitro* (Rice-Evans *et al*., 1996) and antioxidants may protect against CVDs. Hydroxycinnamic acids are the major classes of phenolic compounds, which are found in almost every plant (Herrmann, 1976; Kuhnau, 1976). The polyphenolic compounds were shown to have beneficial effects in preventing cardiovascular alterations in NO-deficient hypertension (Pechanova *et al*., 2004). Sinapic acid, a phenolic acid is a cinnamic acid derivative, which possesses 3,5-dimethoxyl and 4-hydroxyl substitutions in the phenyl group of cinnamic acid. It is widely

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distributed in the plant kingdom and is obtained from various sources such as rye, fruits and vegetables (Andreasen *et al*., 2001). It has already been pharmacologically evaluated for its antioxidant (Roy and Prince, 2012; Roy and Prince, 2013), antihyperglycemic (Kanchana *et al*., 2011), peroxynitrite scavenging (Zou *et al*., 2002), anti-inflammatory (Yun *et al*., 2008) and neuroprotective effects (Kim *et al*., 2010). Therefore, in the present study we investigated the effects of sinapic acid on heart rate, enzymatic antioxidants and lipid level in L-NAME induced hypertensive rats.

MATERIALS AND METHODS

Animals and chemicals

Healthy male albino Wistar rats (180-220g), were obtained 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 ± 3 °C)with a 12 h light/12 h dark cycle. Feed and water were provided *ad libitum* to all the animals. The study protocols were approved by the Institutional Animal Ethics Committee of Rajah Muthiah Medical College and Hospital (Reg No. 160/1999/CPCSEA, Proposal number: 926), Annamalai University, Annamalainagar. Nω-Nitro-L-arginine methyl ester hydrochloride (L-NAME) and sinapic acid (SA) were purchased from Sigma-Aldrich (St. Louis, Missouri, USA). All other chemicals used in this study were of analytical grade obtained from Merck and Himedia, India.

L-NAME induced hypertensive animal model and sinapic acid treatment

Animals were given L-NAME in drinking water at a dosage of 40 mg/kg body weight for 4 weeks. Sinapic acid was dissolved in corn oil (vehicle) and administered to rats orally everyday using an intragastric tube for 4 weeks.

Experimental protocol

Different doses of sinapic acid (10, 20 and 40 mg/kg/body weight (bw)) were assessed to find out the antihypertensive effect in L-NAME-induced hypertension.

Group I: Control+vehicle
Group II: Control+sinapic acid (40 mg/kg bw)
Group III: L-NAME control (40 mg/kg bw)
Group IV: L-NAME+sinapic acid (10 mg/kg bw)
Group V: L-NAME+sinapic acid (20 mg/kg bw)
Group VI: L-NAME+sinapic acid (40 mg/kg bw)

The experimental duration was 30 days. On 31st day, the rats were anaesthetized and sacrificed by cervical dislocation. Blood samples were collected into heparinized tubes. After the separation of plasma, the buffy coat, enriched in white cells, was removed and the remaining erythrocyte was washed three times with physiological saline. A known volume of erythrocyte was lysed with hypotonic phosphate buffer at pH 7.4. The hemolysate was separated by centrifugation at 350 × g for 10 min and the supernatant was used for the estimation of enzymatic antioxidants.

Preparation of tissue homogenates

Heart and aortic tissues were excised immediately and rinsed in ice-cold normal saline. A portion of the tissue was weighed, homogenized in 0.1 M Tris–HCl buffer (pH 7.4) solution. The homogenate was centrifuged and the supernatant was used for the estimation of various biochemical parameters.

Blood pressure measurement

Before commencement of the experiment, animals were trained with instrument for measuring blood pressure. In all groups of animals, heart rate was measured every week during the entire period of the study noninvasively using a tail cuff method (IITC, model 31, USA) according to standard procedures. Values reported are the average of three sequential measurements. All the recordings and data analyses were done using a computerized data acquisition system and software.

Determination of enzymatic antioxidants

Superoxide dismutase (SOD) activity was assayed in the erythrocyte and tissues by the method of Kakkar *et al*. (1984). Erythrocytes (0.5 ml) were diluted to 1.0 ml with distilled water followed by addition of 2.5 ml of ethanol and 1.5 ml of chloroform (all reagents chilled) was added. This mixture was shaken and then centrifuged. The enzyme activity in the supernatant was determined. The assay mixture contained 1.2 ml of sodium pyrophosphate buffer, 0.1 ml of phenazine methosulphate, and 0.3 ml of nitroblue tetrazolium and appropriately diluted enzyme preparation in a total volume of 3 ml. The reaction was started by the addition of 0.2 ml of nicotinamide adenine dinucleotide (NADH). After incubation at 30 °C for 90 s, the reaction was arrested by the addition of 1.0 ml of glacial acetic acid. The reaction mixture was stirred vigorously and shaken with 4 ml of n-butanol. The mixture was allowed to stand for 10 min; centrifuged and n-butanol layer was separated. The color density of the chromogen in n-butanol was measured at 510 nm against butanol blank. The activity of catalase (CAT) in the erythrocyte was assayed by the method of Sinha (1972). To 0.9 ml of phosphate buffer, 0.1 ml of erythrocyte and 0.4 ml of H_2O_2 were added. The reaction was arrested after 60 s by adding 2 ml of dichromate–acetic acid mixture. The tubes were kept in a boiling water bath for 10 min and the color developed was read at 620 nm. The activity of glutathione peroxidase (GPx) in the erythrocyte was measured by the method of Rotruck *et al*. (1973). To 0.2 mL of Tris buffer, 0.2 ml of ethylene diamine tetraacetic acid (EDTA), 0.1 ml of sodium azide, and 0.5 ml of erythrocyte were added. To the mixture, 0.2 ml of glutathione followed by 0.1 ml of H_2O_2 was added. The contents were mixed well and incubated at 37 °C for 10 min along with a tube containing all reagents except the sample. After 10 min, the reaction was arrested by the addition of 0.5 ml of 10% TCA. The tubes were centrifuged and the supernatant was used for the estimation of glutathione.

Estimation of total cholesterol

Tissue lipids were extracted by the method of Folch *et al*. (1957) using chloroform: methanol mixture (2:1 v/v). The

levels of total cholesterol (TC) was estimated by the method of Zlatkis *et al*. (1953). Lipid extract of 0.5 ml was evaporated to dryness. To this, 5.0 ml of ferric chloride-acetic acid reagent was added. The tubes were mixed well and 3.0 ml of concentrated sulphuric acid (H_2SO_4) was added. A series of standards containing cholesterol in the range 3–15µg were made up to 5.0 ml with the reagent and a blank containing 5.0 ml of the reagent were prepared. The absorbance was read after 20 minutes at 560 nm.

Estimation of triglycerides

The content of triglycerides (TG) was estimated by the method of Fossati and Prencipe (1982). Lipid extract of 0.5 ml was evaporated to dryness. To this, 0.1 ml of methanol was added followed by 4.0 ml of isopropanol. About 0.4 g of alumina was added to all the tubes and shaken well for 15 minutes. It was centrifuged and then accurately 2.0 ml of the supernatant was transferred to appropriately labeled tubes. The tubes were placed in a water bath at 65 °C for 60 minutes for saponification after adding 0.6 ml of the saponification reagent followed by 0.1 ml of sodium metaperiodate and 0.5 ml of acetyl acetone reagent. After mixing, the tubes were kept in a water bath at 65 °C for an hour. A series of standards of concentration 8–40 µg triolein were treated similarly along with a blank containing only the reagents. All the tubes were cooled and read at 405 nm.

Estimation of free fatty acids

Free fatty acid (FFA) level was estimated by the method of Falholt *et al*. (1973). An aliquot (0.5 ml) of the lipid extract was evaporated to dryness. To this, 1.0 ml of phosphate buffer, 6.0 ml of extraction solvent, and 2.5 ml of copper (Cu-TEA) reagent were added. All the tubes were shaken vigorously for 90 seconds and were kept aside for 15 minutes. Then the tubes were centrifuged and 3.0 ml of the upper layer was transferred to another tube containing 0.5 ml of diphenylcarbazide solution and mixed carefully. The absorbance was read at 550 nm after 15 minutes. A reagent blank containing (1.0 ml) of phosphate buffer was processed as blank.

Estimation of phospholipids

Phospholipid (PL) level was estimated by the method of Zilversmit and Davis (1950). An aliquot of 0.5 ml of the lipid extract was pipetted out into a Kjeldahl flask and evaporated to dryness. To the extract, 1 ml of 5 N H_2SO_4 was added and digested in a digestion rack till the appearance of light brown color. Two to three drops of concentrated nitric acid was added and the digestion continued till it became colorless. The Kjeldahl flask was cooled and 1.0 ml of distilled water was added and heated in a boiling water bath for about 5 minutes. Then, 1.0 ml of 2.5% ammonium molybdate and 0.1 ml of 1-amino-2-napthol-4-sulfonic acid were added. The volume was then made upto 5.0 ml with distilled water and the absorbance was measured at 660 nm within 10 minutes.

Histopathology of heart and aorta

Heart and aortic tissues obtained from all experimental groups were washed immediately with 0.9% saline and then fixed in 10% buffered formalin. After fixation, the tissues were processed by embedding in paraffin wax. Then, the tissues were sectioned (5–6 µm thickness) using a microtome and stained with hematoxylin and eosin (H&E) dye. Sections were examined under a high power microscope (Nikon ECLIPSE TS 100; Japan) and photomicrographs were taken.

Statistical analysis

Data were analyzed by one-way analysis of variance (ANOVA) followed by Duncan's multiple range test (DMRT) using statistical package for the social science (SPSS) software version 20.0. Values were expressed as mean ± S.D. for six rats in each group. Values were considered significant when $P<0.05$.

RESULTS

Effect of SA on heart rate and water intake

Figs. 1 and 2 shows the effect of SA on heart rate and water intake in control and L-NAME induced hypertensive rats. Heart rate and water intake were increased significantly ($P<0.05$) in L-NAME induced hypertensive rats when compared with control. Treatment with SA (10, 20, & 40 mg/kg) significantly ($P<0.05$) reduced the heart rate and water intake in L-NAME induced hypertensive rats. The 40 mg/kg dose showed better effect in reducing heart rate and water intake than other two doses (10 and 20 mg/kg), and also in our previous study the 40 mg/kg dosage showed higher effect, so we have chosen 40 mg/kg dosage for further evaluation.

Table 1. Effect of sinapic acid (SA) on SOD, CAT and GPx in erythrocytes of various experimental groups

Parameter		Control	Control+SA	L-NAME	L-NAME+SA
SOD	Erythrocytes (U^a/mg Hb)	7.15 ± 0.51	7.21 ± 0.45	3.76 ± 0.69*	6.09 ± 0.31$^{\#}$
CAT	Erythrocytes (U^b/mg Hb)	172.1 ± 9.44	174.2 ± 7.23	101.3 ± 6.18*	152.19 ± 7.27$^{\#}$
GPx	Erythrocytes (U^c/mg Hb)	14.8 ± 0.65	14.3 ± 0.85	7.25 ± 0.43*	11.8 ± 0.71$^{\#}$

U^a, enzyme concentration required to inhibit the chromogen produced by 50% in one minute under standard condition. U^b, µmol of H_2O_2 consumed/minute. U^c, µg of GSH utilized/minute. Values are mean ± S.D. for six rats in each group. Data were analyzed by one-way ANOVA followed by Duncan's multiple range test (DMRT). $^*P<0.05$ compared with the control. $^{\#}P<0.05$ compared with the L-NAME.

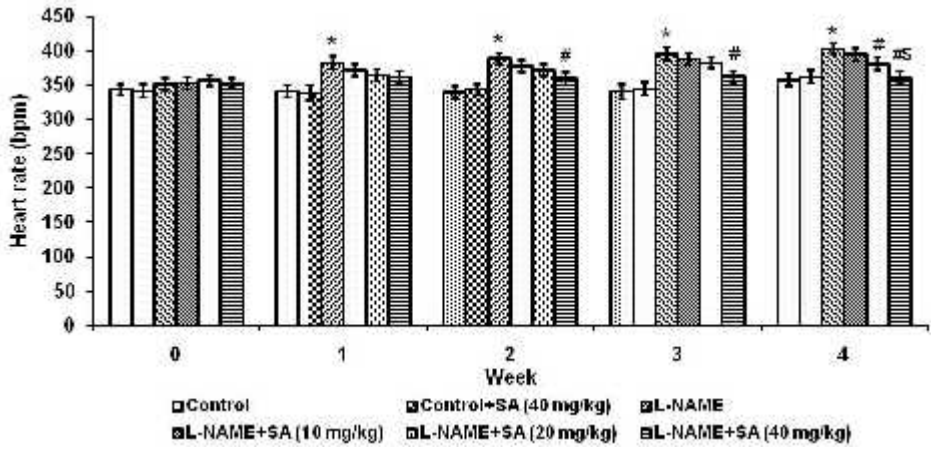

Fig. 1. Effect of sinapic acid (SA) on heart rate in various experimental groups

Columns are mean ± S.D. for six ratsin each group. Data were analyzed by one-way ANOVA followed by Duncan's multiple range test (DMRT). *P<0.05 compared with the control. #P<0.05 compared with the L-NAME. $ P<0.05 compared with the SA (20 mg/kg) group.

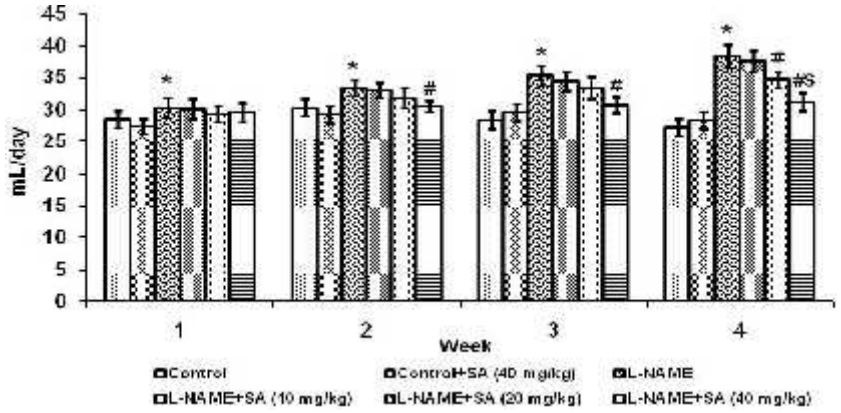

Fig. 2. Effect of sinapic acid (SA) on water intake in various experimental groups

Columns are mean ± S.D. for six ratsin each group. Data were analyzed by one-way ANOVA followed by Duncan's multiple range test (DMRT). *P<0.05 compared with the control. #P<0.05 compared with the L-NAME. $ P<0.05 compared with the SA (20 mg/kg) group.

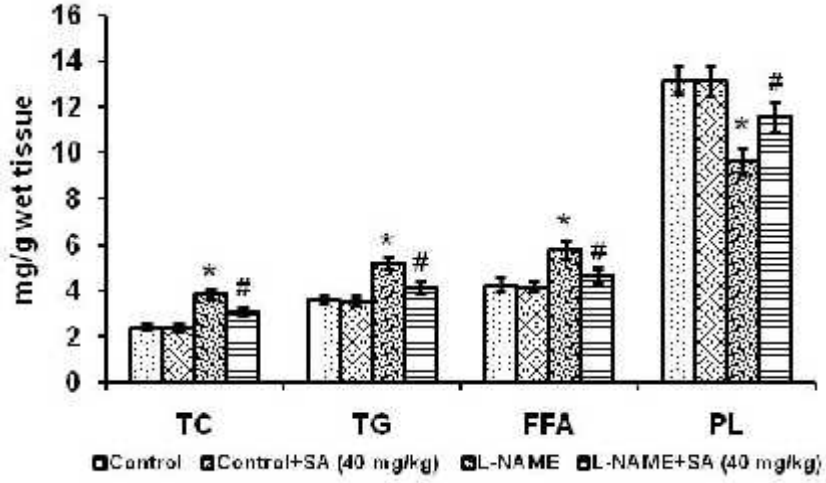

Fig. 3. Effect of sinapic acid (SA) on lipid profile in heart of various experimental groups

Columns are mean ± S.D. for six ratsin each group. Data were analyzed by one-way ANOVA followed by Duncan's multiple range test (DMRT). *P<0.05 compared with the control. #P<0.05 compared with the L-NAME.

Effect of SA on enzymatic antioxidants

The activities of superoxide dismutase, catalase and glutathione peroxidase in erythrocytes of control and L-NAME hypertensive rats are presented in Table 1. The activities of these enzymatic antioxidants were significantly ($P<0.05$) decreased in L-NAME hypertensive rats. Treatment with SA significantly ($P<0.05$) restored the activity of these enzymatic antioxidants in erythrocytes of L-NAME hypertensive rats.

Effect of SA on cardiac and aortic lipids

Figs. 3 and 4 depict the levels of lipids (TC, TGs, FFAs, and PLs) in heart and aorta of control and L-NAME hypertensive rats.

The levels of lipids (TC, TG and FFA) were significantly ($P<0.05$) increased and the level of PL was significantly ($P<0.05$) decreased in L-NAME hypertensive rats when compared to control rats. Treatment with SA significantly ($P<0.05$) declined the levels of TC, TG and FFA, and increased the level of PL in L-NAME hypertensive rats.

Histopathology of heart

Fig. 5(A-D) shows the effect of sinapic acid on the histology of heart in normal and L-NAME induced hypertensive rats. Normal untreated rats showed normal cardiac fibers (Fig. 5A). Normal rats treated with sinapic acid (40 mg/kg) showed normal cardiac muscle bundle without any damage (Fig. 5B).

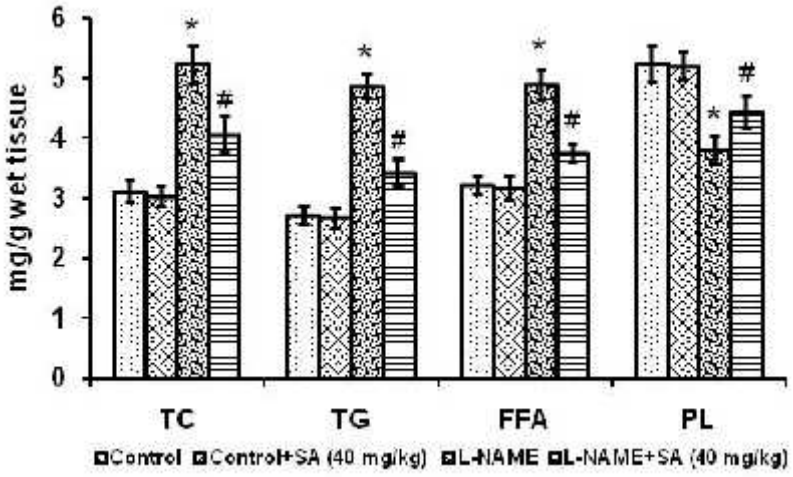

Fig. 4. Effect of sinapic acid (SA) on lipid profile in aorta of various experimental groups

Columns are mean ± S.D. for six ratsin each group. Data were analyzed by one-way ANOVA followed by Duncan's multiple range test (DMRT). *P<0.05 compared with the control. #P<0.05 compared with the L-NAME.

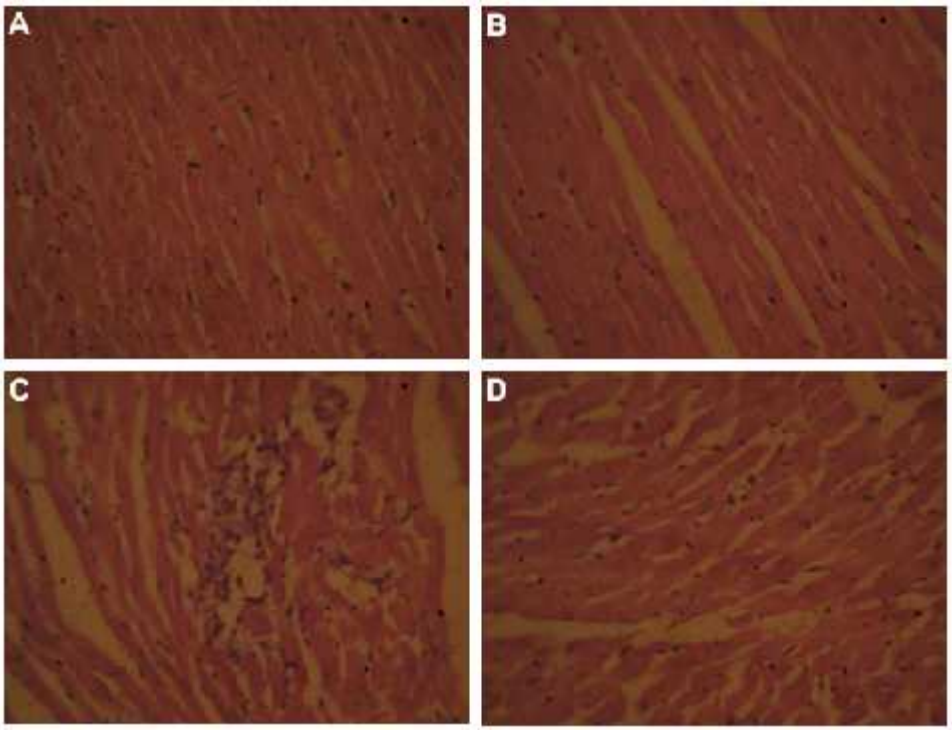

Fig. 5. Representative photomicrograph of histological changes in heart of various experimental groups

(A) Control, cardiac muscle fiberslooks normal. (B) Control+ sinapic acid (40 mg/kg), also shows normal architecture of muscle fibers. (C) L-NAME, there was focal mononuclear cellular infiltrate with rupture of muscle fibres. (D) L-NAME + sinapic acid (40 mg/kg), shows cardiac (not hypertrophic) muscle fibers.

Fig. 5C shows the histopathological finding of L-NAME induced heart with focal mononuclear cellular infiltrate with rupture of muscle fibres. Sinapic acid (40 mg/kg) treated L-NAME hypertensive rats shows not hypertrophic cardiac muscle fibers (Fig. 5D).

Histopathology of aorta

Fig. 6(A-D) shows the effect of sinapic acid on the histology of aorta in normal and L-NAME induced hypertensive rats. Histopathological observations of control aorta revealed normal layers (Fig. 6A). SA supplementation (40 mg/kg) to control rats did not have any changes in the aorta (Fig. 6B). Fig. 6C represents the aortic section from L-NAME hypertensive rats, which exhibits thickening of the vessel wall. The above alteration was reduced in aorta of rats treated with SA shows aortic wall with minimal thickening (Fig. 6D).

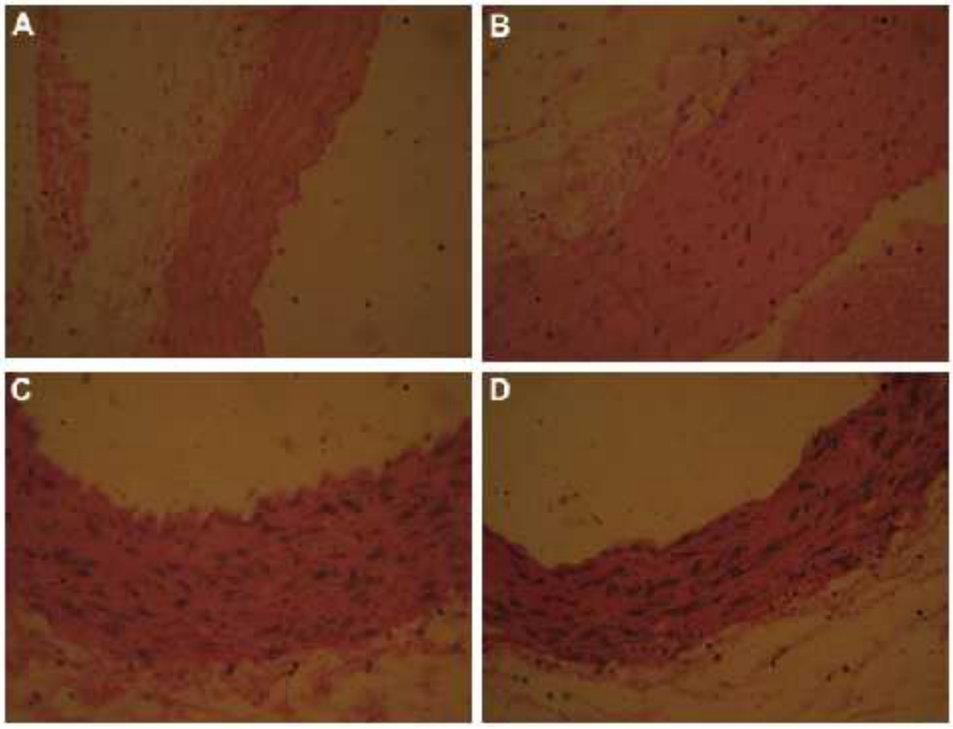

Fig. 6. Representative photomicrograph of histological changes in aorta of various experimental groups

(A) Control, aortic wall looks normal. (B) Control+ sinapic acid (40 mg/kg), also shows normal architecture. (C) L-NAME, there was thickening of the vessel wall. (D) L-NAME + sinapic acid (40 mg/kg), aortic wall with minimal thickening.

DISCUSSION

Endothelium dependent vasorelaxation is responsible for the production of several vasoactive substances, one of the most vital of which is NO, a potent vasodilator synthesized from L-arginine by the enzyme endothelial NOS (Roberts *et al*., 1999). NO synthase inhibition produces hypertension, endothelial damage, cardiac hypertrophy, inflammation, atherosclerosis, ventricular contractile dysfunction, and fibrosis (Moncada *et al*., 1991). Besides, it is well established that chronic inhibition of NO biosynthesis by *in vivo* administration of L-NAME, an L-arginine analog, leads to arterial hypertension and renal vasoconstriction (Jover *et al*., 1993). Several studies related to experimental hypertension showed that an increase in arterial blood pressure reduces circulatory nitric oxide, which reflects the role of arginine–nitric oxide in the pathophysiology of hypertension (Dryden *et al*., 2005). Previous studies reported that the phenolic compounds reduce blood pressure and prevent target organ damage in hypertensive rats (Jalili *et al*., 2006). In this study, L-NAME-treated rats showed significantly increased heart rate and water intake. Treatment with SA significantly reduced the heart rate and water intake due to its antihypertensive property (Silambarasan and Raja, 2014). Oxidative stress can damage many biological molecules; indeed, proteins and DNA are often more significant targets of oxidative injury than lipids, and lipid peroxidation often occurs late in the injury process. It occurs when there is a serious imbalance between the generation of reactive oxygen species (ROS) and the antioxidant defense systems in the body (Maxwell, 1995). The loss of the balance between oxidation and antioxidation may lead to promote the generation of OH• which is a powerful oxidant for many compounds. Crucial components of the antioxidant defense system in the body are cellular antioxidant enzymes, which play a primary role in the maintenance of a balanced redox status.

Free radical scavenging enzymes such as SOD, CAT and GPx (Sawyer *et al*., 2002) are the first line cellular defense against oxidative stress. SOD plays an important role in scavenging superoxide anion, which is the initial free radical, among the oxygen radicals. Catalase prevents oxidative hazard by catalyzing the formation of water and oxygen from hydrogen peroxide (Rajeshkumar and Kuttan, 2003). GPx offers protection to the cellular and subcellular membranes from the

peroxidative damage by eliminating hydrogen peroxide by utilizing reduced glutathione and H_2O_2 as substrates to yield H_2O and oxidized glutathione and its declined activity may be due to the reduced availability of GSH (Li *et al*., 2012). Our previous study shows that the levels of TBARS and LOOH were increased in L-NAME hypertensive rats, whereas treatment with SA lowered the levels of lipid peroxidation products (Silambarasan and Raja, 2014). In the current study activities of SOD, CAT and GPx were decreased in the erythrocytes of L-NAME hypertensive rats. A possible explanation for the decreased enzymatic antioxidant system in circulation may be due to their increased utilization in the neutralization of reactive oxygen species. Previous reports explored the protective effect of sinapic acid on enzymatic antioxidant system (Pari and Jalaludeen, 2011). In consistent with the previous report, in this study sinapic acid treatment enhanced the activities of SOD, CAT and GPx in hypertensive rats.

The blockade of NO synthase by L-NAME seems to be involved in lipid metabolism alterations: increases serum/plasma cholesterol levels in rats (Khedara *et al*., 1996) and impairs endothelium function in hypercholesterolemic rabbits (Cayatte *et al*., 1994). The presence of high blood pressure (BP) and hyperlipidemia is so common in hypertension that many have argued that the high BP itself may play a role in altering lipid metabolism, resulting in abnormalities (Friedwald *et al*., 1972). Hypercholesterolemia and hypertriglyceridemia were seen in nitric oxide-deficient rats which might be due to increased mobilization of lipids from liver and kidney tissues (Saravana kumar *et al*., 2010; Saravana kumar and Raja, 2012). Elevated total cholesterol (TC) levels augment the risk of cardiovascular disease associated with hypertension. Elevated cholesterol levels predispose to a condition known as hypercholesterolemia. Large epidemiologic studies have demonstrated that subjects with hypertension have a marked increase in the prevalence of hypercholesterolemia (Yang *et al*., 2011). Treatment with SA lowered the levels of total cholesterol in tissues of hypertensive rats clearly indicate the antioxidant potential of SA in protecting nitric oxide from free radicals thereby increasing the availability.

Hypertension frequently coincides with elevated levels of triglycerides (TGs). Very low density lipoprotein-cholesterol (VLDL-C) is the major transport vehicle for the TGs from the liver to extrahepatic tissues, whereas low density lipoprotein-cholesterol (LDL-C) is not secreted as such the liver; rather, it seems to be formed from VLDL-C after partial removal of TGs by lipoprotein lipase (Mayes, 1997). 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 (Casazza *et al*., 2009). Finally treatment with SA affected triglyceride levels positively in tissues of L-NAME hypertensive rats. This effect clearly exposed the lipid lowering property of SA. Fatty acids play a key role in the formation and maintenance of all cells and PL are the major structural components of intracellular membranes in all living organisms. Abnormalities in fatty acids and phospholipid metabolism are important in the pathogenesis of cell membrane dysfunction (Saravana kumar *et al*., 2010). Such lipid-dependent modifications of membrane properties in cells participating in the cardiovascular regulation might be a part of pathogenetic mechanisms responsible for chronic blood pressure elevation (Isselbachner *et al*., 1999). Elevated level of FFA was attenuated by sinapic acid treatment in L-NAME rats could be due to inhibition of intestinal absorption of cholesterol, alteration of endogenous cholesterol metabolism (Yotsumoto *et al*., 1997). The major targets of damaging free radicals are the cellular and membrane phospholipids. L-NAME rats showed decreased phospholipid content in tissues could be due to an accelerated degradation of membrane phospholipids by phospholipases (Farber and Young, 1981). Treatment with sinapic acid protects tissues from lipid peroxidation by mopping up free radicals and decreased the levels of FFAs and increased phospholipids level in tissues of L-NAME hypertensive rats. This effect revealed the anti-lipid peroxidation property of sinapic acid (Silambarasan and Raja, 2014).

Major findings from the present study demonstrated that sinapic acid supplementation could effectively prevent the development of hyperlipidemia in L-NAME rats. Our findings also illustrate that the heart and aorta damage was ameliorated by sinapic acid supplementation.

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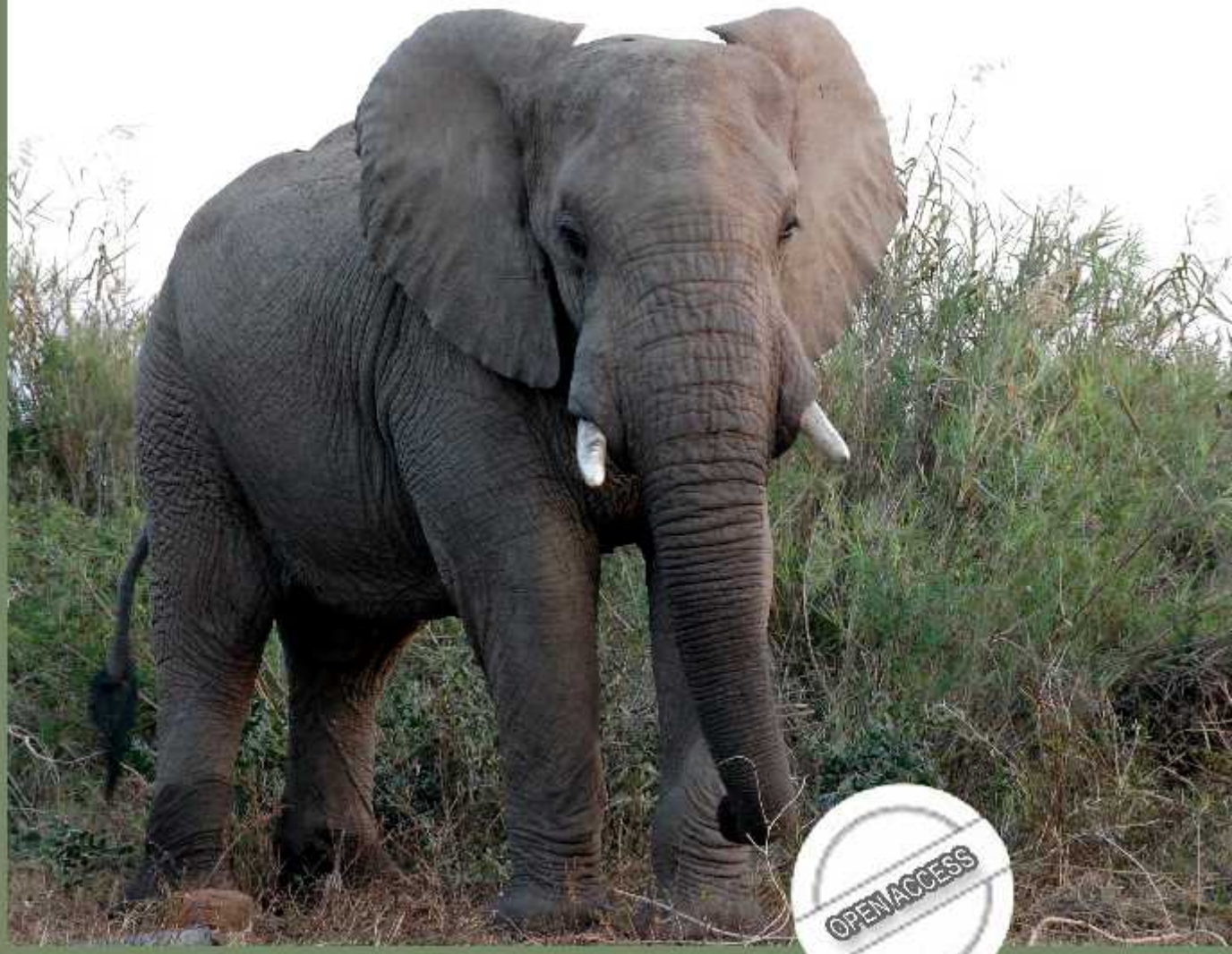

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