STUDY OF CARDIOPROTECTIVE AND ANTIHYPERTENSIVE EFFECTS OF CARDONARC SYRUP-AN AYURVEDIC PROPRIETARY MEDICINE IN FRUCTOSE INDUCED HYPERTENSION IN RATS.

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ABSTRACT

An experimental study was conducted to evaluate the antihypertensive, antilipidemic and cardioprotective potentials of Cardonarc syrup- an Ayurvedic proprietary medicine in fructose induced hypertensive and cardiotoxic rats. Albino Sprague Dawley rats (24 male) were equally divided into 4 groups. Group I served as normal control. Hypertension and cardiotoxicity was induced in the remaining groups with the administration of fructose (10% w/v) p.o ad libitum daily for 6 weeks. Cardonarc syrup (4.8ml/kg p.o) and Pioglitazone 10mg/kg p.o administered daily for three weeks (4th, 5th and 6th week) to the group III and IV respectively. The ECG, HR and invasive BP and the serum biomarkers- CK, CK-MB, LDH, Lipid Profile: (TC, VLDLc, HDLc, TG) and heart tissue biomarker SOD were estimated in all the rats. The histological observations of cardiac tissue also studied. The results of the present study enunciated that Cardonarc has potent antihypertensive, antilipidemic and cardioprotective potential activities in restoring the pathological alterations in fructose induced hypertensive, cardiotoxic rats. Pioglitazone used as standard drug.

Key words- Cardonarc, Pioglitazone, Cardiotoxicity, Hypertension, Sprague Dawley.

INTRODUCTION

Hypertension is the most common cardiovascular illness and is a major public health issue in developed as well as in developing countries. Deaths due to hypertension arise from cerebrovascular and cardiovascular complications such as stroke, end-stage renal disease, congestive heart failure, myocardial infarction and cardiac arrest. Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths. Fructose induced hypertension model gives clue about the role of dietary changes in hypertension. High fructose or high sucrose diets have been documented to increase blood pressure in
Mechanism underlying fructose induced hypertension is that excess fructose in dietary regime can lead to chronic stimulation of sympathetic nervous system primarily as a result of increased insulin levels. This over activation of SNS in return exacerbates insulin resistance which results in a positive feedback mechanism. Several allopathic medications are available for hypertension treatment. But because of life threatening side effects for instance synthetic antihypertensive like diuretics cause muscle cramps, dehydration, extreme tiredness, skin rash, blurred vision and abnormal heart rate, ACE inhibitors cause cough, kidney failure, skin rash and fever, calcium channel blockers cause fatigue, skin rash, constipation and edema, β-blockers cause bronchospasm, Reynaud’s syndrome, heart failure and postural hypotension, as β-blockers cause bronchospasm so contraindicated in asthma, others like centrally acting drugs cause sexual dysfunction. In addition, all antihypertensive drugs are contraindicated during pregnancy except methyldopa. Cardonarc syrup is an Ayurvedic proprietary medicine which is formulated by Vasishta Pharmaceuticals Pvt Ltd, Bengaluru and claims to have antihypertensive effect. Nowadays, herbal formulations have gained popularity due to the associated side effects that comes along with the usage of allopathic medicines. Therefore, our current research work was done to evaluate the cardioprotective and antihypertensive effects of Cardonarc syrup.

**MATERIALS AND METHODS**

**Drugs and Chemicals:** Cardonarc, Pioglitazone, Fructose, Heparin, Normal Saline, Ketamine hydrochloride, Xylazine, Triton X, Nitro blue-tetrazolium, Sodium Carbonate, Hydroxylamine Hydrochloride, di Sodium EDTA, di Potassium Hydrogen Phosphate, Potassium di hydrogen Phosphate.

**Biochemical Kits:** HDL, Total cholesterol, triglyceride, CK, CK-MB, LDH.

**Animals:** 24 Male Sprague Dawley rats were procured from Adita Biosys Pvt. Ltd. Bangalore. They were obtained in healthy condition with the health certificate provided from the suppliers and verified by the veterinarian. These animals were then housed in stainless steel cover and polystyrene box cages and allowed free access to water and feed and kept in 12h light and 12h dark cycle. The base of the cages was covered with 1-2cm thick husk layer which was changed on a regular basis of thrice per week. The temperature in the animal house was regulated at 22-24˚C by air conditioning and a relative humidity of the 65% measured by the hygrometer in the animal house was maintained. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC, Approval No-PESCP/IAEC/38/2016 dated11-6-2016). All animals were maintained under standard conditions prescribed by CPCSEA.

**Experimental design**

The experimental study was carried out on 24 Albino Male Sprague Dawley that were randomly divided into four groups comprising of 6 rats in each group. Group I served as normal control. Group II were administered fructose (10%w/v) p.o ad libitum daily for 6 weeks. Group III rats received cardonarc syrup (4.8ml/kg p.o) daily for three weeks (4th, 5th and 6th week) along with fructose (6weeks). Group IV rats received Pioglitazone 10mg/kg p.o daily for three weeks (4th, 5th and 6th week) along with fructose (6 weeks).

**Blood withdrawal technique and blood processing:** This technique is used when the animal is required to recover in experimental circumstances and this method is commonly known as retro orbital technique and also called periorbital, posterior-orbital and orbital venous plexus bleeding. Blood samples were collected under ether anesthesia 24 h after the last day treatment. The animal was scrubbed within the thumb and forefinger and the skin around the eye was pulled out. A capillary tube was inserted into the medial canthus of the eye at about 30-degree angle to the nose. Slight thumb pressure was applied to puncture the tissue and enter the plexus/sinus. Once punctured the blood automatically comes out through the capillary tube. 1ml of blood was collected from each animal (24 rats) in 4 groups in Eppendorf tubes.

**Separation of serum for Biochemical estimations:** The resultant tubes were kept for incubation in an upright position for a period of 30-45 min to allow clotting. Then it was centrifuged using a cold centrifuge for a period of 15min at 1000-2000 rpm. Using a clean pipette, the supernatant serum was aspirated and poured
into another Eppendorf tube. The serum was used for the estimation of lipid profile, CK-MB, CK, LDH using Erba biochemical kits.

**Estimation of Serum Parameters:** CK, CK-MB, LDH, Lipid Profile: TC, HDL, TG. All these serum biomarkers were estimated as per the method given in the Erba diagnostic kit leaflet.

**Creatinine kinase (CK):** At first, 1000µl of reagent 1 and 40µl of sample is taken, mixed and incubated for 3mins at 37°C. Then the absorbance was measured and at the same time the stopwatch was started. The absorbance was read again exactly after 1, 2 and 3 min. The average was calculated at 1-min absorbance change (ΔA).

**Creatinine Kinase- MB:** 1ml of the reagent 1 (buffer) is taken and mixed with 50µl of the sample and incubated at 37˚C for 3 min. Then reagent 2 or the substrate is added at a quantity of 250µl again mixed and incubated at a temperature of 37˚. Then the absorbance was measured and then again after 1, 2 and 3 min.

**LDH:** Lactate dehydrogenase was estimated by mixing 800µl of reagent 1 with 20µl of the sample in a test tube. For the standard, 800µl of reagent 1 was taken along with 20µl of the standard and for the blank 800µl of reagent 1 and 20µl of distilled water was taken and mixed well, incubated for 1 min at 37˚C. After incubation, 200 µl of reagent 2 was added in each of the test tubes and again mixed and incubated at 37˚C for 1 min then the initial absorbance was measured for the sample, standard and blank.

**Lipid profile Estimation:** Serum Cholesterol- To 1000µl of the working reagent, 20 µl of standard cholesterol (200mg/dl) was added and incubated for 10 min at room temperature. The serum cholesterol was estimated by adding 20 µl of serum sample to 1000 µl of the reagent, mixed well and incubated at room temperature for 10 min. This mixture was aspirated and absorbance was recorded against reagent blank at 505nm using biochemical semi auto analyzer.

**Estimation of Serum HDL:** At first precipitation of LDL, VLDL and chylomicron is done by adding 250µl of the sample and 500µl of the precipitating reagent and mixed well. Then the reaction mixture was allowed to stand for 10 min at room temperature. Then it was centrifuged at 4000 r.p.m (1800 x g) for 10 min. The supernatant was taken to determine the concentration of HDL cholesterol in the sample.

**Estimation of Serum Triglycerides:** To 1000µl of the working reagent, 20 µl of triglyceride (200mg/dl) was added and incubated for 10 min at room temperature. This incubated mixture was aspirated in semi-auto analyzer and the concentration of the standard was calibrated to show a value of 200mg/dl. The serum triglyceride was estimated by adding 20 µl of serum sample to 1000 µl of the reagent, mixed well and incubated at room temperature for 10 min. This mixture was aspirated and absorbance was recorded against reagent blank at 505nm.

**Serum LDL-** The serum LDL amount was calculated by using Friedewald’s formula i.e. LDL=TC-TG/5 – HDL.

**Serum VLDL** The serum VLDL was calculated using formula: VLDL= TG/5

**Measurement of ECG:** An overnight fasted (minimum period of 8–10 h) rat was used in the experiment. The animal was anaesthetized with ketamine (80 mg/kg, i.p. and xylazine (16 mg/ kg, i.p.). The reflexes of the animal were checked, and it is placed on a suitable rodent surgical table or a flat movable surface. The ECG was measured using AD instruments.

**Invasive BP Measurement** - BP measurement is one of the basic procedures in biomedical research. Three methods are most widely used for recording the BP in a rat: (i) tail cuff plethysmography (noninvasive), (ii) intra-arterial catheters (invasive), and (iii) radio telemetry. Intra-arterial catheters yield the most precise values, and surgery is required to use them. Invasive blood pressure (IBP) is the gold standard against which the accuracy of noninvasive blood pressure method (NIBP) is compared. IBP is the arterial pressure directly measured in any artery such as the radial, femoral, or brachial artery using a cannula (saline-filled catheter) .


The carotid artery was located near the vagus nerve. The carotid artery was separated from the nerve using a small needle, and the cephalic end of the blood vessel was tied and the cardiac end was clamped with a bulldog clip. The blood vessel was cannulated using a cannula pre-filled with heparinized normal saline (0.5IU/ml). The other end was connected to a three-way stopcock/saline filled tuberculin syringe. Then the carotid artery was tied with a thread without obstructing the blood flow in the carotid cannula. After this the bulldog clamp at the cardiac end of the blood vessel was released slowly, ensuring that there is no bleeding at the site.

The three-way stopcock was connected to the pressure transducer and a syringe filled with Cannulation for Fig.1 Invasive BP measurements in rats

Recording of BP and Heart rate- After cannulation the animal was connected to the data acquisition system (Power lab) for the recording of BP and Heart rate. After the experiment the rat was sacrificed using a recommended anesthetic agent. And the heart was used of the study of tissue parameters.

Tissue parameters: The animals were sacrificed as per the CPCSEA guidelines and the heart was isolated and weighed. The homogenate was prepared on ice in the ratio of 4g of the tissue with 16 ml of phosphate buffer of pH 7.5 which contained 1mM/l disodium EDTA and 10 ml of 500mM/l BHT in acetonitrile to prevent the formation of new peroxides during the assay. The homogenates were then centrifuged at 4˚C at 2000 gyrations for 20 min. The resultant homogenate was then used for the estimation of SOD. The second half of the heart tissue was used for histopathological study.

Estimation of Superoxide Dismutase (SOD) : Superoxide dismutase was estimated according to the methodology proposed by Kono (1978). In the test cuvette, the reaction mixture containing 1.3 ml sodium carbonate buffer, 500 µl NBT and 100 µl Triton X-100 was taken. The reaction was initiated by the addition of 100 µl hydroxylamine hydrochloride. After 2 min, 70 µl of the enzyme extract was added. The percentage inhibition in the rate of NBT reduction was recorded as an increase in absorbance at 540 nm. SOD activity was expressed as A= U/g tissue.

RESULTS

<table>
<thead>
<tr>
<th>Group</th>
<th>P wave duration (sec)</th>
<th>QRS complex duration (sec)</th>
<th>T wave duration (sec)</th>
<th>RR interval Duration (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0.016±0.0046</td>
<td>0.029±0.0089</td>
<td>0.009±0.0096</td>
<td>0.353±0.2378</td>
</tr>
<tr>
<td>II</td>
<td>0.018±0.0056</td>
<td>0.0308±0.0123**</td>
<td>0.025±0.0066</td>
<td>0.530±0.0187**</td>
</tr>
<tr>
<td>III</td>
<td>0.009±0.0068*</td>
<td>0.035±0.0080</td>
<td>0.031±0.0148</td>
<td>0.437±0.1972*</td>
</tr>
<tr>
<td>IV</td>
<td>0.006±0.0032**</td>
<td>0.063±0.0126</td>
<td>0.033±0.0354</td>
<td>0.601±0.1339</td>
</tr>
</tbody>
</table>

ECG was expressed in seconds in each group and the values were expressed as Mean ± SEM (n = 6) animals in each group. *P<0.05, **P<0.001, is considered as significant when compared to fructose group. ##P<0.001, is
considered as significant when compared to normal group done by Bonferroni’s test comparison of selected columns.

Graphs:

- **P wave duration**
  - Graph showing comparison of P wave duration across different groups: Normal, Fructose, Cardonarc+F, Standard+F.
  - Significant differences indicated by asterisks.

- **QRS complex duration**
  - Graph showing comparison of QRS complex duration across different groups: Normal, Fructose, Cardonarc+F, Standard+F.
  - Significant differences indicated by double asterisks.

- **T wave duration**
  - Graph showing comparison of T wave duration across different groups: Normal, Fructose, Cardonarc+F, Standard+F.
  - Significant differences indicated by single asterisks.
RR Interval

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Fructose</th>
<th>Cardonarc+F</th>
<th>Standard+F</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.0</td>
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</tr>
<tr>
<td>0.8</td>
<td></td>
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</tr>
</tbody>
</table>

ECG of normal rat (group I)

ECG of Group II rats (Fructose treated)

ECG of Group III rat (Fructose + Cardonarc treated)

ECG of Group IV rat (Fructose + Pioglitazone treated)
Table 2. –BP and HR values in normal and treated rats

<table>
<thead>
<tr>
<th>SN</th>
<th>Groups</th>
<th>DAP in mm Hg</th>
<th>SAP in mm Hg</th>
<th>MAP in mm Hg</th>
<th>HR in beats/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal</td>
<td>98.58 ± 2.386</td>
<td>110.6 ± 7.923</td>
<td>102.4 ± 4.031</td>
<td>244.0 ± 18.03</td>
</tr>
<tr>
<td>II</td>
<td>Fructose</td>
<td>114.8 ± 6.543**</td>
<td>130.3 ± 16.19*</td>
<td>120.1 ± 7.200**</td>
<td>320.3 ± 24.26***</td>
</tr>
<tr>
<td>III</td>
<td>Cardonarc + F</td>
<td>103.3 ± 5.750'</td>
<td>111.8 ± 5.563'</td>
<td>106.3 ± 5.017'</td>
<td>196.7 ± 33.36***</td>
</tr>
<tr>
<td>IV</td>
<td>Pioglitazone + F</td>
<td>99.35 ± 10.72''</td>
<td>108.2 ± 13.00''</td>
<td>102.3 ± 11.37''</td>
<td>233.2 ± 37.26***</td>
</tr>
</tbody>
</table>

The blood pressure was expressed in mm of Hg in every group and each value were expressed as Mean ± SEM (n = 6) animals in each group. *p<0.05, ** p<0.001, ***p<0.0001 is considered as significant when as compared to fructose group; #p<0.05, ##p<0.001, ###p<0.0001 is considered as significant when as compared to normal group done by One way ANOVA followed by Bonferoni’s test comparison of selected columns.

Graphs:
**Mean Arterial Pressure**

![Bar chart showing mean arterial pressure with different groups: Normal, Fructose, Cardonarc, and Standard.](chart)

**Heart rate**

![Bar chart showing heart rate with different groups: Normal, Fructose, Cardonarc, and Standard.](chart)

**Fig. No. BP in normal group rat (Group I)**

**Fig. No. BP in Fructose treated rat (Group II)**

**Lipid Profile:** Table showing the lipid profile values in normal and treated rats.

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Each value was expressed as Mean ± SEM (n = 6) animals in each group. **p<0.001, ***p<0.0001 is considered as significant when as compared to fructose group; #p<0.05, ##p<0.001, ###p<0.0001 is considered as significant when as compared to normal group done by One way ANOVA followed by Bonferoni’s test comparison of selected columns.

**Graphs**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Group</th>
<th>Total cholesterol mg/dl</th>
<th>Triglycerides mg/dl</th>
<th>HDL mg/dl</th>
<th>VLDL mg/dl</th>
<th>LDL mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal</td>
<td>43.53±2.040</td>
<td>17.40±4.647</td>
<td>17.17±2.059</td>
<td>3.479±0.9295</td>
<td>22.89±2.937</td>
</tr>
<tr>
<td>2</td>
<td>Fructose</td>
<td>53.30±5.788***</td>
<td>25.02±6.620##</td>
<td>5.945±1.121###</td>
<td>5.004±1.324*</td>
<td>42.35±5.110###</td>
</tr>
<tr>
<td>3</td>
<td>Cardonarc+F</td>
<td>44.02±3.936**</td>
<td>15.73±4.359**</td>
<td>9.493±1.612**</td>
<td>3.146±0.871**</td>
<td>31.38±4.193***</td>
</tr>
<tr>
<td>4</td>
<td>Pioglitazone+F</td>
<td>42.15±3.683***</td>
<td>12.86±2.733***</td>
<td>13.25±2.025***</td>
<td>2.573±0.546***</td>
<td>26.33±4.465***</td>
</tr>
</tbody>
</table>
Results of LDH, CK, CK-MB and SOD.

Table showing the results of LDH, CK, CK-MB and SOD

<table>
<thead>
<tr>
<th>SN.</th>
<th>Group</th>
<th>LDH (IU/L)</th>
<th>CK (IU/L)</th>
<th>CK-MB (IU/L)</th>
<th>SOD (U/g tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal</td>
<td>272.8±31.74</td>
<td>41.88±14.62</td>
<td>14.45±2.699</td>
<td>37.04±1.365</td>
</tr>
<tr>
<td>II</td>
<td>Fructose</td>
<td>312.1±40.27</td>
<td>118.1±5.521###</td>
<td>27.56±5.298###</td>
<td>24.49±1.207##</td>
</tr>
<tr>
<td>III</td>
<td>Cardonarc+F</td>
<td>208.0±11.29###</td>
<td>91.73±7.762###</td>
<td>20.37±2.740**</td>
<td>35.01±1.270***</td>
</tr>
<tr>
<td>IV</td>
<td>Pioglitazone+F</td>
<td>105.9±24.82###</td>
<td>92.73±9.619###</td>
<td>15.65±2.671***</td>
<td>42.18±2.086***</td>
</tr>
</tbody>
</table>

Each value was expressed as Mean ± SEM (n = 6) animals in each group. ** p<0.001, ###p<0.0001 is considered as significant when compared to fructose group; ##p<0.001, ###p<0.0001 is considered as significant when as compared to normal group done by One way ANOVA followed by Bonferoni’s test comparison of selected columns.

**Graphs**

Effect of Cardonarc on LDH

Effect of Cardonarc on CK level

Effect of Cardonarc on CK-MB
Histopathological examination of heart tissue in normal and treated rats

The heart section of normal rat (group I) shown intact arrangement of cardiac muscle fibres. Intact integrity of myocardial cell membrane maintained, and myofibrillar structure with striations and continuity with adjacent myofibrils observed. Intracellular spaces appear intact but vascular spaces were observed to have enlarged. The sections in Fructose treated rats (group II) shown loss in the integrity of the myocardial cell membrane, myofibrillar structure with loss of striations and loss of continuity with adjacent myofibrils. Interstitial spaces near the focal areas seem increased (arrows shown in the figure). The sections in group III (F + Cardonarc treated) rats shown intact arrangement of cardiac muscle fibres. The cardiac muscle fibre shown intact arrangements continuity observed. Interstitial space seems mildly increased (long arrows) Vascular spaces appear congested (small arrows). The sections of the heart in group IV rats (F + Pioglitazone) shown intact arrangement of fibres, unremarkable interstitial spaces. Continuity with adjacent myofibrillar structure and striations were observed.

DISCUSSION

The P wave is the onset of atrial depolarization due to the change in the potential caused by the impulse originated by the SAN. The fructose treated rats (II) shown insignificant increase in the P wave duration when compared to Normal rats (I) and Cardonarc + F and Pioglitazone + F (III and IV) have shown significant decrease in the P wave duration when compared to Gp II control rats. The QRS complex is the onset of ventricular depolarization. Soon after this the ventricle systole begins. The group II rats have shown significant increase in the QRS complex duration when compared to Group I rats but no significant difference was observed in Group III and Group IV rats. The T wave is the onset of ventricular repolarization, soon after this the ventricles start to relax. All group rats showed insignificant difference in the T wave duration. The RR interval duration is the duration required for one cardiac cycle or one ECG. The Group II rats shown
significant increase when compared to Group I rats. Group III rats shown significant decrease when compared to Group II rats.

The Mean Arterial pressure is derived from Systolic Arterial Pressure and Diastolic Arterial Pressure. SAP is the pressure exerted at the time of ventricular ejection. The normal SAP is 120 mmHg. The Diastolic Arterial Pressure is the Pressure exerted by the heart when it is at diastole. The rats treated with Fructose (Group II) has shown significant increase in DAP, SAP and MAP when compared to Normal group (Group I). The group III rats have significant decrease in the above parameters when compared to Group II rats. The Group IV rats also showed significant decrease in the relevant parameters when compared to the Group II rats. The results of these in-vivo measurements of BP suggest the antihypertensive potential of Cardonarc. The fructose induced rats (Group II) have shown significant increase in Heart rate compared to Group I rats. This effect of fructose induced tachycardia may have been caused due to modulation of SAN. The group III rats have shown significant decrease in the heart rate when compared to group II rats. This suggests cardio protective effect of Cardonarc.

The Group II rats have shown significant increase in serum lipid profile- cholesterol, Triglyceride, VLDL and LDL levels when compared to the normal Group I rats. Recent studies reveals that high fructose diets enhance hepatic secretion of VLDL and may decrease its plasma clearance which results in hypercholesterolemia and hypertriglyceridemia (hyperlipidemia). Group III rats (C+F) has shown significant decrease in total cholesterol, TG, VLDL and LDL levels and is almost equal to normal levels. This anticholesterolomic and hypertriglyceridemic effect of Cardonarc is maybe due to the interference in hepatic secretion of VLDL and its plasma clearance. Group IV (P+F) has also exhibited a similar outcome in the levels of the above parameters. The Group II rats have shown decreased HDL cholesterol. Cardonarc (Group III) has shown a significant decrease in total cholesterol, TG, VLDL and LDL levels and is almost equal to normal levels. This anticholesterolomic and hypertriglyceridemic effect of Cardonarc is maybe due to the interference in hepatic secretion of VLDL and its plasma clearance. Group IV (P+F) has also exhibited a similar outcome in the levels of the above parameters.

Group II rats have shown increased HDL cholesterol. Cardonarc (Group III) has shown a significant increase in the HDL level when compared to Group II. The Pioglitazone has also produced a similar result as that of Cardonarc.

Group II rats have shown increase in serum LDH level when compared to Group I rats this effect may be due to Fructose induced increased release of LDH from the cardiac and the liver cells. The Cardonarc Group III rats have shown significant decrease in the LDH level when compared to Group II rats. The standard drug Pioglitazone has also produced similar effect. This report suggests the protective role of Cardonarc in preventing the release of LDH from the cells. Group II has shown significant increase in the serum CK and serum CK-MB levels. Both are the cardiac biomarkers. The increased levels of these biomarkers may indicate the fructose induced cardiotoxicity. Group III rats C+F have shown significant decrease in CK and CK_MB levels when compared to Group II rats. Standard drug Pioglitazone has also shown the same effects. This result indicates the cardioprotective effect of Cardonarc.

Group II rats have shown decreased level of the antioxidant enzyme SOD of heart tissue sample; this is due to extensive utilization of SOD due to oxidative stress caused by fructose in cardiac cells. The Group III rats have shown significant increase in SOD level. When compared to Group II rats. This suggests the anti-oxidant potential of Cardonarc. This may have caused due to the protective role of Cardonarc on fructose induced oxidative stress in the cardiac cells. Group IV pioglitazone treated rats showed similar effects as Cardonarc. From the histopathological sections (heart tissue) of the all four groups it is clearly observed that the damage to the myocardial cells was observed in the fructose only group. Interstitial spaces have increased. Loss of the cardiac cell integrity was observed with loss of continuity and striations in myofibrillar structure. When the group III Cardonarc + fructose group animals were compared to that of Group II animals it has shown fair protection in maintaining the integrity, arrangement, continuity and striation in the myofibrillar structure. So has the standard group animals of Group IV treated with Pioglitazone along with fructose.

CONCLUSION

The results of the study showed that Cardonarc has a pronounced role in decreasing the fructose induced elevated blood pressure levels which was at par with the standard drug used for the study i.e. Pioglitazone. Cardonarc syrup has proved to have a notable role in producing a cardioprotective action by remarkably reducing the levels of myocardial cell damage biomarkers such as LDH, CK, and CK-MB when compared to the disease control group i.e. Group II or Fructose group. The rats treated with cardonarc showed decreased levels
of serum lipid profile - total cholesterol, TG, VLDLc and LDLc levels and increased levels of HDLc when compared to group II control rats confirms the antilipidemic potentials of cardonarc (cardioprotective activity).

The antioxidant enzyme SOD was also found to have decreased in the Cardonarc treated rats when compared to the fructose only treated rats, suggesting its protective role on fructose induced oxidative stress in myocardial cells. Histopathological studies also supported that the cellular structure of the heart was also protected from the damage caused by fructose.

From the results of this study it is concluded that Cardonarc syrup- a herbal Ayurvedic formulation developed by Vasishta Pharmaceuticals Pvt. Ltd, Bengaluru possesses cardioprotective, antilipidemic and antihypertensive effects. The result data has provided useful discernment into the feasibility of using Cardonarc to treat hypertension and cardiac susceptible patients. Future studies aimed at understanding the actual mechanism underlying Cardonarc antihypertensive activity and cardioprotective action is certainly condoned.

Acknowledgements: The authors thank Prof.Dr.J.Saravanan, Principal, Prof.Dr.S.Mohan Director, PES College of Pharmacy and Ms.Vasishta Pharmaceuticals Bengaluru for providing infrastructure and financial facilities for this study.

Conflict of interest: There are no complicit of interest.

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