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Cardioprotective effect of Cranberry extract on isoproterenol-induced myocardial infarction in rats

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ABSTRACT

Myocardial infarction (MI) is characterized by an inequity of coronary blood supply and demand, which results in myocardial ischemic injury and damages the cardiomyocytes. Isoproterenol (ISO) is a synthetic catecholamine found to cause toxicity leading to severe stress in the myocardium of experimental animals. The aim of the present article is to investigate the cardioprotective activity of cranberry extract against ISO-induced cardiotoxicity in adult rats. Oral administration of cranberry extract at a concentration of 75 and 150 mg/kg b.wt. daily for 28 days showed a significant protection against-induced alteration in plasma total cholesterol (TC), triacylglycerols (TG), high density lipoprotein (HDL-C), low density lipoprotein (LDL-C), tumor necroses factor-alpha (TNF-α) and nitric oxide (NO) as well as cardiac superoxide dismutase (SOD), glutathione peroxidase (GPx), reduced glutathione (GSH), catalase (CAT) levels. In addition, cranberry extract reduced plasma Creatine kinase-MB (CK-MB), lactate dehydrogenase (LDH), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) as well as cardiac thiobarbituric acid reactive substances (TBARS) levels as compared to control group. In conclusion, cranberry extract renders resiliency against isoproterenol cardiotoxicity due to its antioxidant and free radical scavenging activity.

Keywords: Cranberry extract, isoproterenol, myocardial infarction, antioxidant and free radical scavenging activity.

1. INTRODUCTION

Cardiovascular disease (CVD) is a major global cause of mortality in the developed countries. Intravascular thrombogenesis, the main pathogenic mechanism of the coronary artery disease (CAD), is influenced by a complex interplay of procoagulant, anticoagulant, fibrinolytic, endothelial damage, dysfunction and inflammatory processes [1]. The traditional theory of causation of CAD centers on a complex interplay between genetic and environmental, modifiable and non-modifiable risk factors setting into motion an inflammatory cascade of monocyte migration, lipid oxidation and atheromatous plaque formation [2]. Isoproterenol is a synthetic catecholamine that has positive inotropic and chronotropic effect. At therapeutic doses it increases cardiac output, however when administered in large doses it was reported to cause severe oxidative stress in the myocardium leading to necrosis of the left ventricular heart muscle [3]. Isoproterenol generates free radicals by the process of auto-oxidation and this free radical mediated oxidative stress was believed to be the mechanistic pathway via which isoproterenol induced necrosis [4]. ISO causes excessive production of free radicals which induce lipid peroxidation (LPO) that causes irreversible damage to the myocardial membrane [5].

Humans have evolved with antioxidant systems to protect against free radicals and ROS. These systems include some antioxidants produced in the body (endogenous) and others obtained from the diet (exogenous) [6]. The first include (a) enzymatic defenses, such as glutathione peroxidase, catalase, and

superoxide dismutase, which metabolize superoxide, hydrogen peroxide, and lipid peroxides, thus preventing most of the formation of the toxic ROS [6]. Plants vegetables and spices used in folk and traditional medicine have gained wide acceptance as one of the main sources of prophylactic and chemopreventive drug discovery and development [7 and 8]. Cranberry ranks high among fruit in both antioxidant quality and quantity [9 and 10] because of its substantial flavonoid content and a wealth of phenolic acids. Cranberry extracts rich in these compounds reportedly inhibit oxidative processes including oxidation of low-density lipoproteins [11 and 12], oxidative damage to at neurons during simulated ischemia [13], and oxidative and inflammatory damage to the vascular endothelium [14]. The antioxidant properties of the phenolic compounds in cranberry fruit may contribute to the observed antitumor activities of cranberry extracts, Plant-derived fraction are rich sources of volatile terpenoids and phenolic compounds [15]. Terpenoids are known to have potential to prevent obesity and have been used in aromatherapy for obese middle-aged women. Phenolic compounds extracted from plants may have antioxidant activity that could mitigate tumor-related complications, including atherosclerosis and some cancers [15-18]. Not surprisingly, plants such as cranberry extract contain high levels of poly-phenols [11 and 15], which are excellent scavengers of reactive and represent a promising renal protective effect. In vivo tests have been conducted with cranberry extract to determine, for example, its hepatoprotective [19], hypolipidemic, hypoglycemic and antioxidant activity [9]. The aim of the present article is to investigate the cardioprotective activity of cranberry extract against ISO-induced cardiotoxicity in adult rats.

2. MATERIALS AND METHODS

2.1 Chemicals and dosage:

2.1.1 The dose of *Cranberry*

Cranberry extract was purchased it from Virgin Extracts (TM), China. *Cranberry* was given to female rat with 1/150 LD_{50} (75mg/kg.b.w.) and 1/75 LD_{50} (150mg/kg.b.w.) daily for 4 weeks by oral gastric gavage tube.

Isoproterenol (100%) and (Vitamin C, 100%) were obtained from Merck Ltd., Germany. All reagents used were of analytical grade and were obtained commercially.

2.2 Experimental Animals:

This experiment was conducted in accordance with guidelines established by the Animal Care and Use Committee of Faculty of Veterinary Medicine, Benha University, Egypt. 60 Adult rats werearound 180±10gms were purchased from National Cancer Institute, Cairo University. They were individually housed in cages in an air-conditioned room with a temperature of 22 ± 2°C, a relative humidity of 60%, and an 8:00 to 20:00 light cycle. During the acclimatization period, each animal was raised on a regular diet adlibitum.

2.3 Experimental set up: This experiment was carried out to examine the biochemical effect of cranberry on induced myocardial infarction. Groups of animals each consisting of 10 rats were treated daily for 28 days as follows.

Group (1): Normal; was given normal diet for 28 days.

Group (2): Positive control; Was given isoproterenol (150mg/kg b.w.) suspended in saline Subcutaneously with a single dose at the 21day.

Group (3): was treated with Cranberry extract (75mg/kg.b.w., orally) daily + isoproterenol (100mg/kg.b.w., orally) suspended in saline Subcutaneously with a single dose at the 21 day [19].

Group (4): was treated with Cranberry extract (100mg/kg.b.w., orally) daily + isoproterenol (100mg/kg.b.w., orally) suspended in saline Subcutaneously with a single dose at the 21 day [19].

Group (5): was treated with Vitamin C (500 mg/kg.b.w) orally daily + isoproterenol (100mg/kg.b.w., orally) suspended in saline Subcutaneously with a single dose at the 21 day [20].

Group (6): was treated with Vitamin C (1000 mg/kg.b.w) orally daily + isoproterenol (100mg/kg.b.w., orally) suspended in saline subcutaneously with a single dose at the 21 day .

At the end of the study, all rats were sacrificed blood was collected, centrifuged, and plasma was used freshly for estimation of CK-MB according to the method of Gerhardt and Waldenström, [21], lactate dehydrogenase (LDH) according to the method of King [22] and transaminases (ALT and AST) activities according to the method of Reitman and Frankel [23] in plasma and heart homogenate were determined using biodiagnostic kits. TNF-α and NO levels were done by the methods described by Beyaert and Fiers [24] and Miranda et al., [25], respectively. Also, TBARs and GSH levels in blood and heart were done by the methods described by Nichans and Samulelson [26] and Chanarin [27], respectively. Blood and heart superoxide dismutase (SOD) and catalase (CAT) activities were carried out Marklund and Marklund [28] and Sinha [29], respectively. Plasma triglyceride, total cholesterol, and HDL- cholesterol were determined using commercially available kits (Asan and Youngdong Pharmaceutical Co., Korea) according to the methods of Fossati and Principe [30]; Allain, [31]; Burnstein et al., [32], respectively. Plasma LDL-cholesterol level was calculated from Friedewald [33] formula (LDL-cholesterol = total cholesterol – triglycerides/5 – HDL-cholesterol).

2.4 Statistical analysis

All the grouped data were statistically evaluated with SPSS/11 software [34]. Hypothesis testing methods included one-way analysis of variance (ANOVA) followed by the least significant difference (LSD) test. *P* values of less than 0.05 were considered to indicate statistical significance. All the results were expressed as mean ± SD for eight separate determinations.

3. RESULTS AND DISCUSSION

Table 1 revealed a significant elevation in plasma cholesterol, triglyceride and low-density lipoprotein (LDL) as well as significant reduction in high-density lipoprotein (HDL) ($p<0.01$) in the second group which represents isoproterenol (100mg/ kg) treated the group of rats compared with control group. The administration of cranberry extract(75 and 150mg/kg.b.w.) and vitamin C(500 and 1000mg/kg BW.) showed significantly decreased in cholesterol, triglyceride and low-density lipoprotein (LDL), as well as significant elevation of high density lipoprotein (HDL) levels relative to isoproterenol, treated group of rats after 4 weeks ($p< 0.01$). Table 2 revealed a significant elevation in plasma aspartate aminotransferase (AST), lactate dehydrogenase (LDH) and creatine kinase-MB (CKMB) activities as well as plasma total protein level ($p<0.01$) in the second group which represents isoproterenol (100mg/ kg) treated the group of rats compared with control group. The administration of cranberry extract (75 and 150mg/kg.b.w.) and vitamin C(500 and 1000mg/kg BW.) showed significantly decreased in AST and LDH activities relative to isoproterenol treated the group of rats after 4 weeks ($p< 0.01$). Tables 3&4 revealed a significant reduction in blood and heart catalase (CAT), glutathione peroxidase (GPx), superoxide dismutase (SOD)and reduced glutathione (GSH) as well as significant elevation of malondialdehyde (MDA) levels ($p<0.01$)in the second group which represents isoproterenol (100mg/ kg) treated group of rats compared with control group. The administration of cranberry extract (75 and isoproterenol (100mg/ kg) treated the group of rats after 4 weeks ($p< 0.01$).

Table 5 revealed a significant elevation in heart tumor necrosis factor-alpha (TNF-α), nitric oxide (NO) and Interleukin-22 (IL-22) gene expression levels ($p<0.01$) in the second group which represents isoproterenol (100mg/ kg) treated the group of rats compared with control group. The administration of cranberry extract (75 and 150mg/ kg.b.w.) and vitamin C(500 and 1000mg/kg BW.) showed significantly decreased in TNF-α and NO activities relative to isoproterenol group of rats after 4 weeks ($p< 0.01$). Also, figures 21and 22revealed a significant depletion in heart total protein and blood hemoglobin levels ($p<0.01$) in the second group which represents isoproterenol (100mg/ kg) treated the group of rats compared with control group.The administration of cranberry extract (75 and 150mg/kg.b.w.) and vitamin C(500 and 1000mg/kg BW.) showed significantly increased in heart total protein and blood hemoglobin levels relative to isoproterenol group of rats after 4 weeks ($p< 0.01$).

Table 1. Effect of Cranberry extract and Vit C. on plasma triglycerides (TG), total Cholesterol (TC), HDL-cholesterol (HDL-C) and LDL- cholesterol (LDL-C) in rats.

No.	Groups	TG (mg/dl)	TC (mg/dl/L)	HDL-C (mg/dl)	LDL-C (mg/dl)
(I)	Normal	115.00 ± 13.48[a]	106.70 ± 13.87[a]	31.20 ± 4.21[a]	52.51 ± 10.25[a]
(II)	Control positive ISO(100 mg/k.b.w.)	175.32 ± 11.82[b]	169.17 ± 15.41[b]	20.16 ± 3.71[b]	113.95 ± 13.63[b]
(III)	ISO (100 mg) + Cranberry extract (75 mg/kg.b.w)	109.48 ±6.84[a]	115.02 ±12.40[a]	29.88 ±4.69[a]	61.58 ±12.43[a]
(IV)	ISO (100 mg) + Cranberry extract (150 mg/kg.b.w)	105.26 ±8.46[a]	108.87 ± 9.90[a]	31.26 ±4.19[a]	56.56 ±11.05[a]
(V)	ISO (100 mg) + Vit. C (500 mg/kg.b.w)	108.99 ±9.94[a]	111.27 ± 9.57[a]	32.69 ±5.87[a]	56.78 ±11.18[a]
(VI)	ISO (100 mg) + Vit. C (1 g/kg.b.w)	113.45 ±9.20[a]	103.68 ± 6.58[a]	33.95 ±4.13[a]	47.04 ± 5.08[c]

Data shown are mean ± standard deviation of number of observations within each treatment. Data followed by the same letter are not significantly different at P ≤ 0.05. Small letters are used for comparison between the means within the column.
LDL-C (mmol/L) = TC-HDL-[TG / 5]

Table 2. Effect of cranberry extract and Vit C plasma activities of Aspartate aminotransferase (AST), Lactate dehydrogenase (LDH),creatine kinase-MB (CKMB)and level of total protein in rats.

No.	Groups	AST (U/L)	LDH (U/L)	CKMB (U/L)	Total protein (g/dl)
(I)	Normal	76.83 ± 7.83[a]	356.67 ± 7.47[a]	85.33 ± 5.09[a]	6.08 ± 0.15[a]
(II)	Control positive ISO (100 mg/k.b.w.)	170.00 ± 5.83[b]	954.00 ± 12.76[b]	343.50 ± 38.89[b]	5.08 ± 0.12[a]
(III)	ISO (100 mg) + Cranberry extract (75 mg/kg.b.w)	153.33 ± 3.56[c]	595.00 ± 10.89[c]	228.33 ± 2.58[c]	5.30 ± 0.14[a]
(IV)	ISO (100 mg) + Cranberry extract (150 mg/kg.b.w)	144.17 ± 3.06[c]	515.83 ± 10.68[d]	214.00 ± 4.86[d]	5.48 ± 0.12[a]
(V)	ISO (100 mg) + Vit. C (500 mg/kg.b.w)	134.83 ±2.32[d]	465.67 ± 6.89[e]	122.50 ± 3.51[d]	5.73 ± 0.12[a]
(VI)	ISO (100 mg) + Vit. C (1 g/kg.b.w)	121.17 ± 2.64[e]	380.00 ± 5.25[f]	99.67 ±7.12[a]	6.15 ± 0.19[a]

Data shown are mean ± standard deviation of number of observations within each treatment. Data followed by the same letter are not significantly different at P ≤ 0.05. Small letters are used for comparison between the means within the column.

Table 3. Effect of cranberry extract and Vit C on blood catalase (CAT), glutathione peroxidase (GPx) and superoxide dismutase (SOD) activities as well as levels of reduced Glutathione (GSH) and plasma thiobarbituric acid reactive substances (TBARS) in rats.

No.	Groups	CAT (U/g Hb)	GPx (U/g Hb)	SOD (U/g Hb)	GSH (mg%)	TBARS (nmol/L)
(I)	Normal	16.36 ± 2.09 [a]	151.39 ± 10.86 [a]	9.00 ± 1.73 [a]	9.28 ± 2.25[a]	4.68 ± 0.91[a]
(II)	Control positive ISO (100 mg/k.b.w.)	6.58 ±1.30[b]	92.78± 14.25[b]	4.28 ± 0.89[b]	3.96 ± 0.54[b]	8.27 ±1.40 [b]
(III)	ISO (100 mg) + Cranberry extract (75 mg/kg.b.w)	11.13 ±1.36[c]	127.36 ±12.31[c]	6.26 ±0.76[c]	6.22 ±1.00[c]	5.47 ±1.06[a]
(IV)	ISO (100 mg) + Cranberry extract (150 mg/kg.b.w)	16.48 ±1.41[a]	148.24 ±10.98[d]	8.24 ±1.12[a]	9.29 ±2.65[a]	4.41 ±0.52[a]
(V)	ISO (100 mg) + Vit. C (500 mg/kg.b.w)	8.35 ±1.48[d]	124.84 ±12.22[c]	6.33 ±0.99[c]	6.01 ±1.62[c]	4.71 ±0.98[a]
(VI)	ISO (100 mg) + Vit. C (1 g/kg.b.w)	14.16 ± 2.25[a]	136.33 ±14.52[d]	8.94 ±0.97[ac]	10.42 ±2.70[a]	4.35 ±0.74[a]

Data shown are mean ± standard deviation of number of observations within each treatment. Data followed by the same letter are not significantly different at P ≤ 0.05. Small letters are used for comparison between the means within the column.

Table 4. Effect of cranberry extract and Vit C on heart catalase (CAT), glutathione peroxidase (GPx) and superoxide dismutase (SOD) activities as well as levels of reduced Glutathione (GSH) and thiobarbituric acid reactive substances (TBARS) in rats.

No.	Groups	CAT (U/mg protein)	GPx (U/mg protein)	SOD (U/mg protein)	GSH (umol/mg protein)	TBARS (nmol/mg protein)
(I)	Normal	11.46 ± 2.41[a]	3.21 ± 0.37 [a]	5.64 ± 0.76[a]	5.64 ± 0.76[a]	51.61 ± 8.87 [a]
(II)	Control positive ISO (100 mg/k.b.w.)	3.5 ± 0.87[b]	1.58 ± 0.35[b]	2.91 ± 0.84[b]	2.73 ± 0.39[b]	96.38 ±10.54 [b]
(III)	ISO (100 mg) + Cranberry extract (75 mg/kg.b.w)	5.40 ±0.69[c]	2.59 ±0.47[c]	4.08 ±0.80[a]	3.70 ±0.67[c]	71.64 ±7.20[c]
(IV)	ISO (100 mg) + Cranberry extract (150 mg/kg.b.w)	11.01 ±1.36[a]	3.42 ±0.66[a]	5.46 ±0.79[a]	5.07 ±0.90[a]	52.40 ±4.30[a]
(V)	ISO (100 mg) + Vit. C (500 mg/kg.b.w)	9.69 ±1.63[a]	2.44 ±0.37 [c]	4.56 ±0.61[a]	4.11 ±0.68[a]	66.65 ±9.41[ac]
(VI)	ISO (100 mg) + Vit. C (1 g/kg.b.w)	10.86 ±1.23[a]	3.35 ±0.48[a]	5.25 ±0.74[a]	4.51 ±0.49[a]	57.69 ± 6.79[a]

Data shown are mean ± standard deviation of number of observations within each treatment. Data followed by the same letter are not significantly different at P ≤ 0.05. Small letters are used for comparison between the means within the column.

Table 5. Effect of Cranberry extract and Vit C. on heart tumor necrosis factor-alpha (TNF-α), nitric oxide (NO), total protein and Interleukin-22 (IL-22) gene expressions well as blood hemoglobin in rats.

No.	Groups	TNF-α (pg/mg protein)	NO (ug/mg protein)	Total Protein (mg/g tissue)	IL-22	Hb% (g/dl)
(I)	Normal	332.62 ± 16.84 [a]	117.53 ± 8.55 [a]	99.38 ± 3.18 [a]	1.03 ±0.03[a]	13.73 ±1.00 [a]
(II)	Control positive ISO (100 mg/k.b.w.)	522.37 ±20.76[b]	158.77 ±7.26[b]	70.90 ±7.92[b]	13.43 ±3.66 [b]	11.10 ±0.51 [a]
(III)	ISO (100 mg) + Cranberry extract (75 mg/kg.b.w)	348.26 ±16.07[a]	139.82 ±10.12[c]	87.69 ±8.94 [ab]	5.63 ±0.48[c]	12.64 ±0.63[a]
(IV)	ISO (100 mg) + Cranberry extract (150 mg/kg.b.w)	345.12 ±17.83[a]	121.01 ±8.72[a]	94.03 ±7.13 [ac]	5.67 ±0.42[c]	13.01 ±0.37 [a]
(V)	ISO (100 mg) + Vit. C (500 mg/kg.b.w)	370.32 ±10.32[c]	131.13 ±7.70[ac]	88.36 ±5.34 [ab]	4.03 ± 1.06[c]	13.33 ± 0.54[a]
(VI)	ISO (100 mg) + Vit. C (1 g/kg.b.w)	349.89 ±16.00[a]	120.81 ±4.53[ac]	96.70 ±10.77 [abc]	3.00 ± 1.39[d]	13.38 ± 0.54 [a]

Data shown are mean ± standard deviation of number of observations within each treatment. Data followed by the same letter are not significantly different at P ≤ 0.05. Small letters are used for comparison between the means within the column.

Oxidative stress has been associated with diverse pathophysiological events, including cancer, renal disease and neurodegeneration [35]. It has been established that excessive oxidative stress caused by either increased ROS production or inadequate antioxidant defenses can lead to cardiac lesions [36]. The present study demonstrates the cardioprotective effect of cranberry extract in isoproterenol-induced cardio toxicity as evidenced by improved antioxidant defense as well as inhibition of lipid peroxidation and prevention of leakage of myocytes injury marker enzymes from heart. Isoproterenol is a widely used chemical in toxicological studies to induce cardiac muscle injury, through an exaggerated pharmacological effect [37]. The administration of isoproterenol is a

well-established animal model of acute myocardial infarction [38].

Lipid peroxidation may also damage membranes in other cells, altering important elements of control for blood pressure and liver rate. Given that increased LDL cholesterol (LDL-C) and decreased HDL cholesterol (HDL-C). Both Britton et al., [39] and Brunet, et al. [40] found the same results. Yates and Dhalla [41] have explained that isoproterenol undergoing oxidation results in the formation of superoxide anion and the chain reactions propagate results in the formation of reactive oxygen species. In the present study, the increased level of oxidative stress markers observed in isoproterenol-injected rats might be due to the generated free radicals from auto-oxidation of isoproterenol.

Since cranberry has shown antioxidant and free radical scavenging activity [42], the present study primarily ameliorating the effect of cranberry' polyphenols on isoproterenol induced heart toxicity in a rat is studied. Oral administration of cranberry extract significantly inverses the isoproterenol induced peroxidative damage in a heart which is evidenced by the lowered levels of thiobarbituric acid reactive substances.

This may be due to the anti-oxidative effect of polyphenols [43]. An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons from a substance to an oxidizing agent. isoproterenol induces cellular injury and functional abnormalities in hepatocytes by the process of lipid peroxidation [44]. Because the heart has a central role in the maintenance of lipid homeostasis, excess iron may alter the concentration of serum lipids, which could reduce or increase the risk of atherosclerosis.

The primary antioxidant enzymes in mammals include SOD which converts superoxide to hydrogen peroxide, GPx, and CAT which are responsible for converting hydrogen peroxide to water [45](Formigari et al. 2007). GSH is a very important non-enzymatic antioxidant which can react directly with free radicals or act as an electron donor in the reduction of peroxides catalyzed by GPx [46](Dringen, 2000). The present results show marked decreased plasma and heart SOD, GPx, CAT and GSH level indicating acute cardiotoxicity in the isoproterenol-treated group. The obtained data in the present study demonstrated that cranberry extract considered as a potent antioxidant agent when given simultaneously with isoproterenol since it could produce marked an increase in plasma and heart SOD, GPx, CAT and GSH levels towards the normal values.

Enzymes, the macromolecules that leak from the damaged tissue, because of their tissue specificity and catalytic activity, are the best markers of tissue damage. Hence, in isoproterenol-induced myocardial infracted rats, there was a decrease in activities of the marker enzymes CK, LDH, AST, and ALT in the heart homogenate, followed by an increase in their levels in plasma [47].

These findings confirm the onset of myocardial necrosis and leaking out of the marker enzymes from a heart to blood [48]. A number of marker enzymes are directly proportional to isoproterenol induced necrotic lesions present in the myocardium. In the present study, pretreatment of cranberry extract to myocardial infarction-induced rats reduce the cardiac damage and restrict the leakage of enzymes as evident from a significant reduction in the activities of cardiac marker enzymes in plasma. In the present study, isoproterenol significantly increased MDA and HP level with concomitant reduction of myocardial CK-MB and LDH enzyme activity. Elevated MDA and HP level reflect an increase in membrane permeability, which could be responsible for the leakage of myocardial enzymes (CK-MB and LDH) from cardiomyocytes [49]. CK-MB and LDH, localized in myocytes, are released during isoproterenol-induced irreversible myocardial injury and are considered as characteristic of cardiac muscle injury [50]. The reduction in the leakage of CK-MB and LDH enzymes from a heart as evidenced by increased levels of CK-MB and LDH in heart tissue is suggestive of the cardioprotective effect of cranberry extract treatment.

Due to disruption of an endogenous antioxidant network, as observed in present study significant increased of TNF-α and NO levels in isoproterenol treated rats compared with negative control group of rats. Isoproterenol induced myocardial toxicity may be more susceptible to free radicals induced ischemic injury and the subsequent cascade of inflammation and injury. Inflammation is the very initial response of the immune system to infection. The anti-inflammatory effect of cranberry extract containing polyphenols has been documented as a good anti-inflammatory Phyto-compounds [19]. The present study findings demonstrate therapeutic benefits of cranberry extract an integrated approach as evidenced by restoration and improvement of TNF-α and nitric NO as well as endogenous antioxidant defense and inhibition of lipid peroxidation. Protective effects of cranberry extract against cardiac toxicity induced by isoproterenol have not been reported earlier to our knowledge, and this study is perhaps the first observation of its kind. In conclusion, our study clearly demonstrates that cranberry extract administration to isoproterenol-induced rats for 28 days possess significant cardioprotection by minimizing the alterations in the activities of the antioxidant enzymes and decreasing the levels of MDA. These effects could be due to membrane protective action of cranberry extract by scavenging the free radicals and its antioxidant action.

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