Original Article

Effect of Curcuma Longa (Turmeric) on Oxidative Stress in Isoproterenol Induced Cardiotoxic Rats

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Abstract

Background: *Cardiotoxicity occurs due to oxidative stress. Traditional spices are well known source of natural antioxidant. Curcuma longa (Turmeric) is a common spice in Bangladeshi cuisines. So, it may be beneficial for cardiovascular diseases.*

Objective: *To assess the effect of Curcuma longa on oxidative stress in isoproterenol induced cardiotoxic rats.*

Material and Methods: *Twenty-one Wistar albino male rats, aged 85 to 100 days; weighing 125±25g (initial body weight) were selected for the study. After acclimatization for 14 days, the rats were divided into three groups. Group A (base line control group), Group B (isoproterenol treated control group) and Group C (ethanolic extract of Curcuma longa pretreated and isoproterenol treated group). On the 10th day of experiment, the rats were sacrificed after taking final body weight. Blood samples were collected from the heart. The heart was removed and weighed. Serum malondialdehyde (MDA) level was estimated by Spectrophotometric method. The statistical analysis was done by SPSS version 22.0.*

Results: *In this study, the mean heart weight and mean heart weight-body weight ratio were non significantly higher but the mean serum MDA ($P<0.001$) level was significantly higher in Group B in comparison to those of Group A. Again, the mean heart weight ($P<0.01$), mean heart weight-body weight ratio ($P<0.05$) and serum MDA ($P<0.01$) levels were significantly lower in Group C than those of Group B.*

Conclusion: *From the result, it can be concluded that Curcuma longa may have antioxidant effect on cardiotoxic rats.*

Keywords: *Curcuma longa, Oxidative stress, Cardio toxicity, MDA*

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Introduction

Cardiotoxicity occurs due to direct effect of the drug on the heart but also an indirect effect due to alterations of hemodynamic flow or due to thrombotic events[1]. As a result, electrophysiological dysfunction of heart and myocardial injury occurs. The causes of cardiotoxicity are the unintended and undesirable consequences of chemotherapeutics (e.g. doxorubicin, cisplatin etc), adverse effects of ingested heavy metals (e.g. lead, cadmium etc), incorrect administration of drug (e.g. high dose of isoproterenol, adrenaline etc.) and some natural cardiotoxins (e.g. cobra venom) [2].

Oxidative stress is an imbalance between generation of reactive oxygen species (ROS) and impaired removal of ROS by antioxidant defense system of the cell or both. As a result of normal metabolic process, free radicals are continuously produced in the body. The antioxidant defense mechanisms of the body combat the adverse effects of these free radicals[3]. These free radicals generate a variety of relatively stable products like Malondialdehyde (MDA). Therefore, serum MDA is an indirect measure of free radical activity in the body and can be considered as a biomarker of oxidative stress. It induces lipid peroxidation of the cell membrane which amplifies cellular damage[4]. Oxidative stress has been associated with a number of diseases such as cardiovascular diseases, neurologic diseases, malignancies, renal diseases, diabetes, skin diseases, aging, respiratory diseases, liver diseases and various types of viral infections[5].

Isoproterenol (ISP) is a β-adrenergic agonist and a chemically synthesized catecholamine that induces cardiotoxicity by generating free radicals[6,7]. These free radicals, especially, reactive oxygen speciesplay an important role in the pathogenesis of oxidative myocardial damage resulting cardiac malfunctions[8]. ROS have been implicated in various cardiovascular disorders including ischemia/ reperfusion (I/R), atherosclerosis, hypertension, cardiotoxicity induced by drugs etc[9].

Spices and herbs are popular resources of natural antioxidants that prevent oxidative stress induced diseases like diabetes, cancer and coronary heart disease. Thus, an adequate intake of antioxidant by consumption of antioxidant rich foods can prevent the development of oxidative stress[10,11].Many natural plant foods and cardioprotective herbal medicines are commonly used in preventing and treating cardiovascular diseases[12].

Curcuma longa (Turmeric) is an herbal plant of the family Zingiberaceae. In traditional Indian medicine, the powder of Curcuma longa uses for the treatment of biliary disorders, anorexia, coryza, cough, diabetic wounds, hepatic disorders, rheumatism and sinusitis[13]. Curcuma longa contains a group of polyphenolic compounds named curcuminoids, consisting of three bioactive analogs-curcumin (curcumin I), demethoxycurcumin (curcuminII) and bisdemethoxycurcumin (curcumin III)[14]. Among them, the main active compound is curcumin which have a wide range of biological effects including anti-inflammatory, antioxidant, antitumour, antibacterial, and antiviral activities[15].

Some researchers observed that heart weight and heart weight/body weight ratio were significantly increased with no significant alteration of body weight in rats treated with ISP (85mg/kg, subcutaneously) daily for 2 consecutive days. In cardiotoxic rats, heart weight and heart weight/body weight ratio might be increased due to interstitial oedema and severe myofibrillar degeneration with infiltration of neutrophil[16]. Some other observed that MDA level was significantly increased in rats treated by ISP with same dose and duration. Increased level of MDA in ISP treated rats indicated increased lipid peroxidation in heart tissue[17].

Some other investigators demonstrated the cardioprotective effect of curcumin against doxorubicin induced myocardial toxicity in albino rats. Here curcumin (active compound of Curcuma longa) significantly decreased the heart weight, heart

weight/body weight ratio and MDA level in curcumin pretreated cardiotoxic rats. They observed that curcumin pretreatment recovered normal structural and architectural integrity of cardiomyocytes and decreased lipid peroxidation in heart tissues[18].

Cardiovascular diseases increasing day by day in our country due to urbanization. Cardioprotective drugs are available in modern medicine but very costly and associated with a number of side effects. So, cost-effective management of CVD should be made available for public interest. Therefore, on the basis of this background the present study was designed to evaluate the antioxidant effect of Curcuma longa on oxidative stress in isoproterenol induced cardiotoxic rats.

Materials and Methods

This prospective experimental study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from January to December 2015.This study was approved by Ethical Review Committee (ERC) of Dhaka Medical College, Dhaka.

Procurement and maintenance of animals:

Total twenty-one Wistar albino male rats, weighing 125±25gwere selected for the study and collected from the animal house of Department of Pharmacy, Jahangirnagar University, Savar, Dhaka. The rats were kept in metallic case in the animal house of Institute of Nutrition and Food Science, University of Dhaka. These rats were acclimatized 14 days in a standard laboratory condition on a 12/12 hour light/dark cycle. They had free access to food and water. Total study period was 23 consecutive days.

Grouping and dose schedule:

After acclimatization, the rats were divided into 3 groups (A,B and C). Each group consisted of 7 rats. Initial body weight of all the rats was measured on 1st day of experiment. In addition to basal diet, the rats were treated as follows: (Table I)

Collection of blood and heart sample:

On the 10th day of experiment, after taking final body weight all the rats were deeply anaesthetized by 30% chloroform and sacrificed. 5ml of blood samples were collected by cardiac puncture of each rat. The supernatant serum was collected after centrifugation of blood. Serum Malondialdehyde (MDA) level was estimated by spectrophotometric method[19]. After removal, the heart was washed in ice cold saline, wiped by tissue paper and weighed by electronic weighing scale.

Statistical analysis:

The results were expressed as mean ± SD. Statistical analysis was done by one way ANOVA followed by Bonferroni post hoc test. In the interpretation of results, *p* value <0.05 was considered as significant.

Results

The initial and final body weights of all the rats were almost similar and showed no statistically significant difference among the groups. (Table II).The heart weight was higher in group B, comparison to that of group A which was not significant. Again, this level was significantly (P<0.01) lower in group C than that of group B. However, there were no significant differences between group A and group C (Figure 1).

The mean heart weight/body weight ratio was higher in-group B in comparison to that of group A which was not significant. The ratio was significantly (P<0.05) lower in group C, comparison to that of group B. But this change showed no significant difference among group A and group C (Figure 2).

The mean serum MDA level was significantly (P<0.001) higher in group B, than that of group A. It was also higher in group C than that of group A but the level was not significant. Again, this level was significantly (P<0.01) lower in group C, in comparison to that of group B (Figure 3).

Table I: Grouping and dose schedule for different groups of rats (N=21)

Groups	Treatment	Route	Dose (per kg body weight)	Duration
A (n=7)	NS	oral	1ml	for 9 consecutive days
B (n=7)	ISP	s.c.	150 mg	on 8th and 9th day
C (n=7)	EECL and ISP	EECL (oral) ISP (s.c.)	EECL 200mg ISP 150 mg	EECL for 9 consecutive days and ISP on 8th and 9th day

NS= Normal saline; ISP= Isoproterenol hydrochloride; EECL= ethanolic extract of Curcuma longa; s.c.= subcutaneous; N= total number of rats; n= number of rats in each group

Table II: Initial and final body weight in different groups of rats (N=21)

Groups	Body weight (gm)	
	Initial body weight (I)	Final body weight (F)
A (n=7)	127.14 ± 14.96	122.85 ± 11.12
B (n=7)	127.14 ± 11.12	112.85 ± 11.12
C (n=7)	115.71 ± 13.97	111.71 ± 10.67

N= total number of rats; n= number of rats in each group

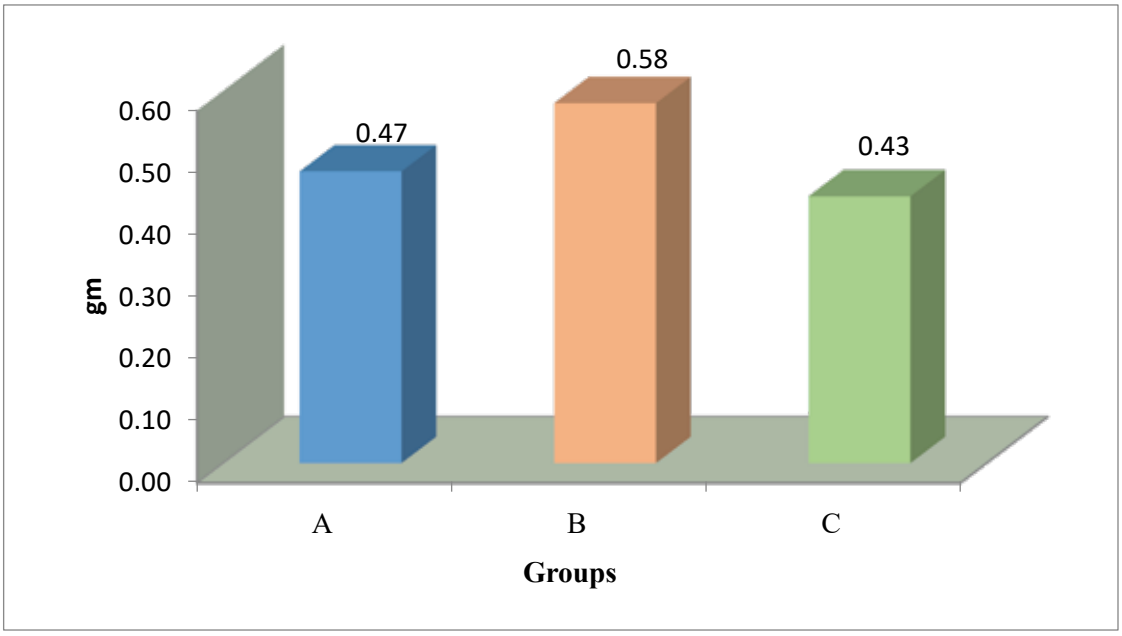

Figure 1: Mean heart weight in different groups of rats (N=21)

Values are means ± SD. Statistical analysis was done by one way ANOVA followed by Bonferroni post hoc test. For heart weight (P<0.01 B vs C). A= normal saline treated group, B= Isoproterenol treated group C= Ethanolic extract of Curcuma longa pretreated and Isoproterenol treated group

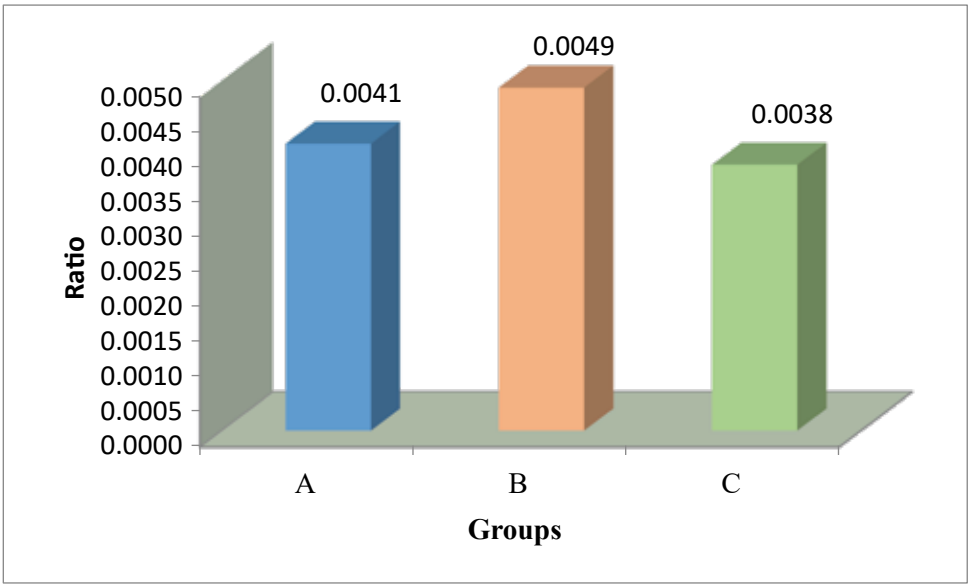

Figure 2: Mean heart and body weight ratio in different groups of rats (N=21)

Values are means ± SD. Statistical analysis was done by one way ANOVA followed by Bonferroni post hoc test. N= Number of rats. For heart and body weight ratio (P<0.05 B vs C). A= normal saline treated group, B= Isoproterenol treated group C= Ethanolic extract of Curcuma longa pretreated and Isoproterenol treated group.

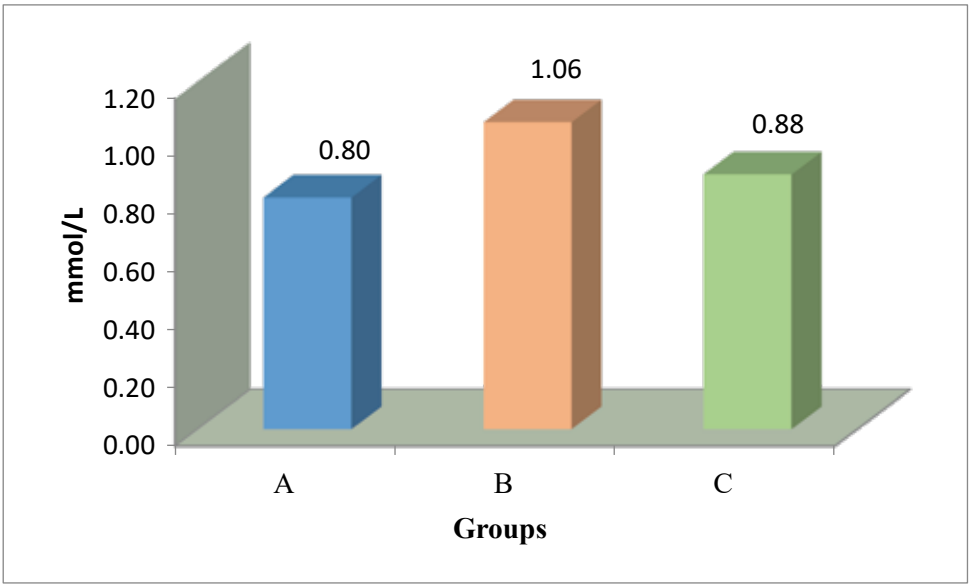

Figure 3: Mean MDA level in different groups of rats (N=21)

Values are means ± SD. Statistical analysis was done by one way ANOVA followed by Bonferroni post hoc test. N= Number of rats. For serum MDA (P<0.001 A vs B), (P<0.01 B vs C). A=normal saline treated group, B= Isoproterenol treated control group C= Ethanolic extract of Curcuma longa pretreated and Isoproterenol treated group.

Discussion

In the present study, the initial and final body weights of all the rats were almost similar and showed no statistically significant difference among the groups. Again, the heart weight and heart weight/body weight ratio were higher in isoproterenol treated control group in comparison to that of baseline control group. However, these levels were significantly lower in isoproterenol treated control group when compared with Curcuma longa pretreated and isoproterenol treated group. Almost similar findings were made by the different investigators but they use curcumin instead of Curcuma longa[20,21].

This study also revealed that, serum MDA level was significantly higher in isoproterenol treated control group in comparison to that of baseline control group. Again, this level was significantly lower in isoproterenol treated control group in comparison to that of Curcuma longa pretreated and isoproterenol treated group. Different researchers of other countries observed almost similar findings by using doxorubicin induced cardiotoxic rats[22].

It has been postulated that, subcutaneous injection of ISP in experimental animals causes increase in heart weight and heart weight/ body weight ratio. The heart weight and heart weight/ body weight ratio were increased due to cardiac hypertrophy. ISP induced cardiac hypertrophy occurs as a result of myocardial oedema, myocytes necrosis, myofibrilar degeneration and leukocyte infiltration[23,24]. However, the rats pretreated with curcumin significantly decrease heart weight and heart weight/body weight ratio in isoproterenol induced myocardial injury which provides an evidence of cardioprotection[20].

Some researchers suggested that large doses of catecholamine undergo auto-oxidation and produce oxidized free radicals. These oxidized catecholamine radicals cause oxidative stress which stimulates lipid peroxidation. Malondialdehyde is a marker of lipid peroxidation and its level correlates with the degree of lipid peroxidation and oxidative stress. Due to these, there are functional hypoxia, intracellular Ca^{2+} overload, coronary spasm and increased membrane permeability resulting increased level of serum cardiac enzymes and MDA[25,26]. Some other investigators recommended that Curcuma longa has free radical scavenging capacity due to its phenolic compounds (e.g. flavonoids and curcuminoids). These are natural antioxidants because of their ability to chelate the transition metal involved in the production of reactive oxygen species via the Fenton reaction. This high antioxidant activity of curcuma longa inhibits lipid peroxidation and ultimately decreases MDA level[27, 28].

In the present study, isoproterenol induced oxidative stress in cardiotoxic rats was evidenced by increased heart weight, heart weight/body weight ratio and higher serum MDA level. Again, decreased heart weight, heart weight/body weight ratio and lower serum MDA level were observed in Curcuma longa pretreated and isoproterenol treated group compared to isoproterenol treated control group. Therefore, it has been demonstrated that Curcuma longa has antioxidant effect, which is most possibly due to inhibition of lipid peroxidation of myocardial cell membrane and its free radical scavenging activity.

Conclusion

From the present study, it can be concluded that Curcuma longa can prevent oxidative stress in isoproterenol induced cardiotoxicity in rats. So, it could be used as natural antioxidant agent that reduces cardiovascular diseases.

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