Myocardial salvaging effect of turmeric (*Curcuma longa*) on experimentally induced myocardial injury in rats

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Abstract

Background: In Ayurveda turmeric (*Curcuma longa*) has been used for cardioprotection. Experimentally induced myocardial injury is clinically similar to human myocardial infarction.

Objective: The study was designed to assess the myocardial salvaging effect of turmeric (*Curcuma longa*) on experimentally induced myocardial injury in rats.

Methods: This experimental study was carried out in the Department of Physiology, Dhaka Medical College, Dhaka during 2015. Total twenty eight (28) Wistar albino male rats (aged 13±1 weeks; 125±25 gm) were randomly grouped into NS (normal control group), ISO (isoproterenol treated control group), Tm+ISO (turmeric pretreated and isoproterenol treated group) and Am+ISO (amlodipine pretreated and isoproterenol treated group). All the rats were sacrificed on 10th day of experimentation. Blood samples were collected. Serum cardiac troponin I (cTnI) level was estimated by AxSYM method and serum malondialdehyde (MDA) level was estimated by spectrophotometric method. For statistical analysis, one way ANOVA followed by Bonferroni post hoc test was done by using SPSS 22.0 version.

Results: The mean serum cTnI and MDA level was significantly (P<0.001) higher in ISO in comparison to all other rats of different groups. Whereas, the mean serum cTnI level was lower in Tm+ISO and Am+ISO in comparison to that of ISO which were statistically significant (P<0.05). Again, mean serum MDA level was significantly lower
In Tm+ISO (P<0.05) and Am+ISO (P<0.001) in comparison to that of ISO. However, there were no significant differences between Tm+ISO and Am+ISO. **Conclusion:** The results of the study concluded that turmeric has myocardial salvaging effect on experimentally induced myocardial injury in rats.

**Keywords:** Turmeric, Cardioprotective, cTnI, MDA

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**Introduction**

Isoproterenol hydrochloride (ISO), a well-known β-adrenergic agonist has positive inotropic and chronotropic effects on the heart. At supramaximal doses, these positive inotropic and chronotropic effects of ISO cause depleted myocardial energy stores. As a result, biochemical and structural changes occurs that may be liable to myocardial injury. It has been well accepted that supra maximal doses of ISO is applied to induce myocardial infarction in experimental animals. ISO induced MI occurs due to excessive production of highly cytotoxic free radicals by an autoxidation process. These free radicals subsequently produce oxidative stress due to reduced endogenous antioxidant activity. Reduced endogenous antioxidant level in the cardiomyocyte leads to impairment of metabolic and contractile action, alteration in the membrane permeability. As a result, lipid peroxidation and irreversible myocardial membrane injury occurs.

Cardiomyocyte has large amount of polyunsaturated fatty acids in its membrane phospholipids. In cardiomyocyte membrane, MDA is a main end product of lipid peroxidation. Increased MDA content indicates oxidative stress which causes necrosis of myocardial tissues in isoproterenol induced animals. Cardiac Troponin I (cTnI) is a specific marker that is generally used for the detection of myocardial injury. It plays a significant role in muscle contraction, and released from the cardiomyocytes when structural damage of the heart occurs due to ischaemia, cardiotoxic agents, etc.

In the traditional Indian medicinal system many plants have been used for cardioprotection. Ayurveda has identified many plants which possess cardiotonic and cardioprotective effects. Some of them are Allium sativum, Allium cepa, Asparagus recemosus, Caesalpinia bonducella, Cassia fistula, Curcuma longa, Emblica officinalis, Garcinia indica, Hemidesmus indicus, Ocimum sanctum, Phyllanthus amarus, Terminalia arjuna, Trigonella foenum-graecum, Vitis vinifera, Withania somnifera and Zingiber officinalis. These plants exhibit potent antioxidant effects, which might be the mechanism behind their beneficial therapeutic properties.

Turmeric (*Curcuma longa*) is the tuberous rhizome of the *Curcuma longa* plant. Dried turmeric powder is used as a spice. It is a basic ingredient of Bangladeshi and Indian dishes for its color, flavor, and taste. Turmeric contains a yellow colored polyphenolic compound called curcumin. It is a potent antioxidant which can potentially inhibit the generation of reactive oxygen species (ROS). Curcumin has been used as a remedy in Chinese herbal medicines for its anti-oxidant and anti-inflammatory effects for a long time. It also acts as a free-radical scavenger and inhibits lipid peroxidation of membrane phospholipids.

Amlodipine belongs to third generation dihydro-pyridine class of calcium channel antagonist. It has slow onset and relatively long duration of action with minimal effects on cardiac electrophysiology and myocardial contractility. It is used for the treatment of hypertension and angina. It is a peripheral arterial vasodilator that acts directly on vascular smooth muscle causes...
reduction in peripheral vascular resistance and blood pressure. It reduces myocardial ischemic injury by reducing myocardial oxygen demand. The transmembrane influx of Ca$^{++}$ into vascular smooth muscle and cardiac muscle is prevented by amlodipine.\textsuperscript{19-21}

A number of studies have shown that, serum cTnI and cardiac tissue MDA levels were significantly increased in rats treated with ISO.\textsuperscript{22, 23} Cytosolic cTnI is released into the blood stream from the injured tissues when the cell membrane becomes leaky or breached.\textsuperscript{24} Myocardial necrosis occurs as a result of lipid peroxidation which is expressed by MDA level.\textsuperscript{25} Again, some researchers observed that turmeric (\textit{Curcuma longa}) extracts significantly reversed isoproterenol induced myocardial necrosis by intensification of endogenous antioxidants, preservation of the myocardial antioxidant levels and significant restitution of the altered hemodynamic parameters.\textsuperscript{26} Begum and her coworker\textsuperscript{27} revealed the cardioprotective effect of amlodipine by reducing oxidative stress induced in experimental myocardial infarction. Amlodipine has potent antioxidant effect due to its physiochemical characteristics.\textsuperscript{28}

It is selected as a standard drug for comparison of cardioprotective effect in this study. But, as far as it has been searched, there is no previous information about this comparison was available. Therefore, the present study was designed to observe the myocardial salvaging effect of turmeric (\textit{Curcuma longa}) in experimentally ISO induced myocardial injury in rats.

\textbf{Methods}

This experimental study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from January to December’ 2015. Animal care and experiments were executed in accordance with the guidelines recommended in the ‘The ethical guidelines for experimentation in laboratory animals’ by the Animal Experimentation Ethics Committee (AEEC) of the International Centre for Diarrhoeal Disease Research, Bangladesh\textsuperscript{29} (icddr,b 2002) and the ethical clearance of this study was obtained from Ethical Review Committee of Dhaka Medical College.

\textbf{Procurement and maintenance of animals:}

Total 28 adult healthy Wistar albino male rats (aged 13±1 weeks; weighing 125±25g) were obtained from the animal house of Department of Pharmacy, Jahangirnagar University, Savar, Dhaka. The animals were kept in metallic cage in the animal house of Institute of Nutrition and Food Science, University of Dhaka. They were housed at room temperature (25±2$^\circ$C), under diurnal conditions (12/12 hour light/dark cycle) for acclimatization.\textsuperscript{30} The rats were kept for 14 consecutive days for environmental acclimatization before experimentation. During this period all the rats had free access to food and water.

\textbf{Experimental protocol:}

After acclimatization, the rats were randomly divided into 4 groups of seven rats in each group. In addition to basal diet, the rats were grouped as follows based on treatment: NS group: received normal saline orally (1ml/kg body weight) for 9 consecutive days. ISO group: received isoproterenol subcutaneously (150 mg/kg body weight) on 8th and 9th day. Tm+ISO group: received ethanolic extract of turmeric orally (200 mg/kg body weight) for 9 consecutive days and isoproterenol subcutaneously (150 mg/kg body weight/day) on 8th and 9th day. Am+ISO group: received amlodipine orally (5mg/kg body weight,) for 9 consecutive days and isoproterenol subcutaneously (150 mg/kg body weight,) on 8th and 9th day.

\textbf{Blood collection:}

On 10th day of experiment, rats were deeply anaesthetized by 30% chloroform. Painless death of the deeply anesthetized rats were ensured by
Five (5) ml of blood samples were collected by cardiac puncture of each rat. The supernatant serum was collected after centrifugation of blood. Serum cTnI level was estimated by AxSYM method and serum malondialdehyde (MDA) level was estimated by spectrophotometric method.

**Statistical analysis:**
Results were expressed as mean ±SD. Statistical analysis were done by one way ANOVA followed by Bonferroni post hoc test by using SPSS windows version 22. In the interpretation of results, p value < 0.05 was considered as level of significance.

**Results**
The serum troponin I level was higher in ISO, in comparison to that of NS, which was statistically significant (P<0.001). Again, this level was lower in Tm+ISO and Am+ISO in comparison to that of ISO which were statistically significant (P<0.05). Whereas, no significant difference was found in this level between Tm+ISO and Am+ISO group (Figure 1).

![Figure 1: Mean serum troponin I level in different groups of rats (N=28)](image)

For Troponin I (**P<0.001, NS vs ISO); (*)P<0.05, ISO vs Tm+ISO and ISO vs Am+ISO). NS= Normal saline control group, ISO= Isoproterenol treated control group, Tm+ISO= Turmeric pre-treated and isoproterenol treated group & Am+ISO = Amlodipin pre-treated and isoproterenol treated group.

The serum MDA level was higher in ISO, in comparison to that of group NS, which was statistically significant (P<0.001). Again, this level was significantly lower in Tm+ISO(P<0.05) and Am+ISO(P<0.001) in comparison to that of ISO. However, there were no significant differences between Tm+ISO and Am+ISO. (Figure 2)

![Figure 2: Serum MDH level in different groups of rats (N=28)](image)

MDA (**P<0.001, NS vs ISO); (^P<0.05, ISO vs Tm+ISO); and (^P<0.001, ISO vs Am+ISO). NS= Normal saline control group, ISO= Isoproterenol treated control group, Tm+ISO = Turmeric pre-treated and isoproterenol treated group & Am+ISO = Amlodipin pre-treated and isoproterenol treated group.

**Discussion**
In this study, mean serum cTnI was estimated to assess myocardial injury. Here, the parameter was significantly higher in ISO treated rats in comparison to those of NS. This finding is similar in different animal studies observed by previous researchers. The increased level of cTnI might be due to ISO-induced myocardial damage and leakiness of the cell membrane. Again, this level was significantly lower in Tm+ISO group in comparison to that of ISO group. This finding is consistent with those of some other research worker but they use curcumin instead of turmeric (Curcuma longa). Here, decreased serum cTnI level suggested that curcumin pretreatment...
improved membrane integrity consequently limiting the release of this contractile protein.\textsuperscript{23} Moreover, mean serum cTnI was also significantly lower in Am+ISO group in comparison to that of ISO group, indicating amlodipine can reduce myocardial injury induced by ISO.

The present study revealed that the mean serum MDA level was significantly higher in ISO treated rats in comparison to alolther rats of different groups (NS, Tm + ISO and Am + ISO). The increased levels of MDA suggested generation of large amounts free radicals by auto-oxidation of ISO and initiation of the lipid peroxidation process, causing irreversible injury to myocardial cells.\textsuperscript{6} Turmeric (\textit{Curcuma longa}) pretreatment significantly decreased the serum MDA levels by preventing formation of lipid peroxides from fatty acids in Tm+ISO but the researchers used doxorubicin as a substitute of ISO to induce myocardial injury.\textsuperscript{30} Moreover, this finding is in consistent with those of some other research worker but they use curcumin instead of turmeric (\textit{Curcuma longa}).\textsuperscript{35} Again, amlodipine pretreated rats showed significant decrease in serum MDA level. This finding agree the findings of other investigators but they used tissue homogenate instead of serum.\textsuperscript{27}

In the present study, isoproterenol induced myocardial injury in rats was evidenced by increased serum cTnI and MDA level. Again, decreased serum cTnI and MDA level were observed in turmeric (\textit{Curcuma longa}) pretreated and isoproterenol treated group compared to isoproterenol treated control group suggested turmeric (\textit{Curcuma longa}) could offer protection against myocardial injury.

Therefore, this study suggested that turmeric has significantly prevented isoproterenol induced myocardial injury in rats. The mechanism of prevention might be due to reduced lipid peroxidation of myocardial cell membrane, preservation of myocardial endogenous antioxidants and cardiac biomarker enzymes. However, the exact mechanism cannot be explained as free radical concentration produced by ISO and phytochemical contents of turmeric were not assessed in the present study.

**Conclusion**

The present study reveals that ethanolic extract of turmeric (\textit{Curcuma longa}) has myocardial salvaging effect on isoproterenol induced myocardial injury by preserving the integrity of myocardial cell membrane and by reducing oxidative stress. Thus, it can recomended to be used as a cardioprotective agents for the prevention of myocardial cell injury against oxidative stress.

**Conflict of interest** - None.

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**References**


