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CARDIOPROTECTIVE POTENTIAL OF *TRIDAX PROCUMBENS* AGAINST ISOPROTERENOL INDUCED MYOCARDIAL INFARCTION IN EXPERIMENTAL RATS

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ABSTRACT

Myocardial infarction is one of the major killer diseases among industrialized nations. Various medicinal plants are available that exhibit potential cardioprotective properties. In the present study, the ethanolic extract of *Tridax procumbens* in various concentrations were studied for screening the cardioprotective activity against isoproterenol induced myocardial infarction in albino rats. Serum marker enzymes like Aspartate Transminase (AST), Alanine Transaminase (ALT), Acid Phosphatase (ACP) and Alkaline Phosphatase (ALP), lipid profile, lipoproteins were determined in serum of experimental animals. Since the induction of Myocardial infarction is accompanied by the generation of free radicals, the role of antioxidants in heart tissue has been studied in experimental animals. The ethanolic extract of *Tridax procumbens* showed significant cardioprotective effect by reducing the level of biochemical parameters like marker enzymes, lipid profile and lipoproteins like LDL and VLDL in increasing concentration. Treatment with *Tridax procumbens* considerably restored the levels of antioxidants with increasing concentration. The results clearly demonstrate that the active phytoconstituents present in *Tridax procumbens* ethanolic extract protects myocardium against isoproterenol induced myocardial infarction.

KEYWORDS: Ethanol, isoproterenol, antioxidants, myocardial infarction, markers.

INTRODUCTION

Myocardial infarction (MI) is one of the major killer disease responsible for mortality and morbidity in developing countries. It is characterized by disruption of blood supply to the heart due to occlusion of blood vessels which causes death of myocardium.

The Risk factors of MI are cigarette smoking, obesity, hypercholesterolemia, hyperlipoproteinemia, high low density lipoprotein and low high density lipoprotein, diabetes, high blood pressure, older age, obesity. The onset of symptoms in MI is usually gradual, over several minutes, and rarely instantaneous. The degree of symptoms ranges from none to sudden cardiac death. Some are symptomatic while some others are asymptomatic**.**

Complications of myocardial infarction (MI) include arrhythmias, congestive heart failure, cardiogenic shock, ventricular Aneurysm, pericarditis, Dressler syndrome and pulmonary embolism (Weir *et al*., 2006). Even though there is a momentous progress in approved drugs, MI remains a fatal clinical crisis (Ma *et al*., 2016).

Therefore, there is a need to develop unique and therapeutically efficient drugs for treating MI and current interest has been focused on plant based natural drug treatments due to cheaper economy rate and lesser side effects. Medicinal plants contain active metabolites called phytoconstituents that play a defensive mechanism against several diseases.

Medicinal plants exhibit antioxidant and free radical scavenging potential due to the presence of phenols and flavonoids which may reduce the risk of heart diseases (Miguel *et al*., 2013).

Tridax procumbens Linn. (Asteraceae) commonly known as coat buttons or tridax daisy in English and Vettukkaaya thalai in tamil is a small perennial herb having short and hairy blade like leaves found along roadsides, waste grounds, dikes, riverbanks and meadows. Traditionally, it is used for the treatment of bronchial catarrh, dysentery, malaria, diarrhea, high blood pressure and to check haemorrhage from cuts, bruises and wounds and to prevent falling of hair (Rajaram *et al*., 2013).The extract of *Tridax procumbens* also possesses anti-diabetic effect (Bhagwat *et al*., 2008) haemostatic activity (Kale *et al*., 2010) and cardiovascular effects (Salahdeen *et al.*, 2004).

The present study was designed to evaluate the cardioprotective potential of *Tridax procumbens* against isoproterenol induced myocardial infarction.

MATERIALS AND METHODS

Collection of plant

The leaves of *Tridax procumbens* was collected from the local villages around Tiruchirappalli and was authenticated by plant taxonomist, Department of Botany, St.Joseph's College, Tiruchirappalli.

The collected leaves were washed thoroughly with water, rinsed with distilled water to remove soil and foreign material if any. The plant was shade dried and powdered. About 1 g of the powdered material was then subjected to extractions using Soxhlet apparatus using ethanol for 6 hours. The extract was finally filtered and used for analysis.

Animals

Healthy albino male wistar rats weighing between 150-200g were used for the study after securing the ethical clearance from Institutional Animal Ethical Committee. The animals were divided in to five groups (n=6).

Experimental Design

Group I: Control ((normal rats received 0.9 % saline)

Group II: received Isoproterenol subcutaneously twice (85mg/kg SC) at an interval of 24 hours.

Group III: received Isoproterenol (85mg/kg SC) and *Tridax Procumbens* Ethanolic Extract (100 mg/kg body weight orally) for 15 days.

Group IV: received Isoproterenol (85mg/kg SC) and *Tridax Procumbens* Ethanolic Extract (200 mg/Kg body weight orally) for 15 days.

Group V: received Isoproterenol (85mg/kg SC) and *Tridax Procumbens* Ethanolic Extract (300 mg/Kg body weight orally) for 15 days.

The animals were sacrificed by cervical decapitation and blood was collected and separated. The heart was dissected and washed in ice cold saline, homogenized and used for various experiments.

Biochemical Assessment in Serum

Estimation of serum markers:

Blood samples were taken and serum was separated for analysis of different cardiac biomarkers like aspartate transaminase (AST), alanine transaminase (ALT), acid phosphatase (ACP) and alkaline phosphatase (ALP).

Estimation of Lipids

Among lipids, total cholesterol, triglycerides, Phospholipids, free fatty acids were determined in serum of experimental animals.

Estimation of Lipoproteins

Lipoproteins like LDL, VLDL and HDL were also estimated in serum of experimental animals.

Biochemical Assessment in Tissue

Estimation of Antioxidant Enzymes

The heart tissue was homogenized in 10% ice cold phosphate buffer (pH = 7) and the mixture was centrifuged and supernatant was collected for analysis of antioxidants like SOD, Catalase, Glutathione peroxidase and Glutathione reductase.

Statistical Analysis

The statistical analysis was performed by ANOVA under one way classification followed by Bonferroni multiple comparison test, changes were considered significant at the P-value of < 0.05 level of significance. The values were expressed as mean ± SD.

RESULTS AND DISCUSSION

The serum marker enzymes such as AST, ALT, ACP and ALP were analyzed in the serum of different groups of experimental animals (Table I). Significant increase was noticed in the serum of isoproterenol (Group II) treated rats when compared to control rats (group I). The increase in isoproterenol treated rats might be due to enhanced susceptibility of myocardial cell membrane to peroxidative damage there by resulting in increased release of serum markers from heart tissue which is similar to the results reported by Raju *et al* (2008). Cotreatment with *Tridax procumbens* in different concentrations brought back the normal level by decreasing the level of markers in serum of isoproterenol administered rats. The presence of phytochemicals with significant antioxidant property decreased the activity of marker enzymes as reported by Malaya gupta *et al*., (2002).

Table I: Effect of marker enzymes in different experimental groups Values are expressed as mean±SD for 6 rats in each group.

Groups	AST(IU/L)	ALT(IU/L)	ACP(IU/L)	ALP(IU/L)
I	24.89 ± 0.67	75.75 ± 0.67	34.70±1.71	186.56 ± 1.67
II	47.60 ± 0.42*	189.65 ±1.06*	54.47± 0.21*	289.23 ± 2.59*
III	38.74 ± 0.24**	86.87 ± 0.51**	35.68 ±0. 14**	230.67 ± 1.05**
IV	30.66 ± 0.56**	85.89 ± 0.25**	45.00 ±0. 25**	214.98 ± 2.18**
V	29.45 ± 0.78**	82.78 ± 1.67**	39.52 ± 1.56**	209.21 ± 1.38**

Statistically significant variations at P<0.05* group II vs group I, ** group III, IV, V vs group II.

Table II represented the level of total cholesterol, triglyceride, free fatty acids, and phospholipids in serum of experimental animals. The serum level of total cholesterol, triglyceride, free fatty acids and phospholipids was significantly increased in isoproterenol administered Group II rats when compared to control rats. Isoproterenol induced myocardial necrosis showed alterations in membrane permeability and loss of function of myocardial membrane (Todd *et al*., 1980). Cotreatment with *Tridax* procumbens in increasing concentration significantly altered the increased levels compared to group II rats. The beneficial effect of *Tridax procumbens* indicates the lipotropic activity and inhibitory effect on lipid peroxidation.

High levels of circulating cholesterol along with TG in heart tissue leads to atherosclerosis, which results in blockage of coronary arteries, interruption of blood supply to parts of heart, leading to death of myocardium (Gokkusu and Mostafazadeh, 2003). Medicinal plants exhibit potent hypolipidemic effect which may be due to the presence of active phytoconstituents (Devi and Sharma, 2004).

Table II: Effect of lipid profile in different experimental groups.
Values are expressed as mean±SD for 6 rats in each group.

Groups	Cholesterol (mg/dl)	Triglycerides (mg/dl)	Free fatty acids (nmoles/mg/protein)	Phospholipids (mg/dl)
I	60.78 ± 0.39	68.37 ± 0.29	45.06 ± 0.31	8.99 ± 0.05
II	165.94 ± 0.34*	179.13 ± 0.53*	80.79 ± 0.38*	15.69 ± 0.37*
III	136.88 ± 0.35**	134.43 ± 0.49**	70.77 ± 0.31**	13.31 ± 0.19**
IV	98.28 ± 0.59**	101.98 ± 0.65**	58.01 ± 0.38**	11.81 ± 0.19**
V	68.97 ± 0.32**	76.32 ± 0.55**	47.00 ± 0.32**	9.37 ± 0.04**

Statistically significant variations at P<0.05* group II vs group I, ** group III, IV, V vs group II.

Figure I showed the level of lipoproteins in serum of experimental animals. In isoproterenol induced rats there was a significant increase in LDL and VLDL followed by decrease in HDL level when compared to control rats. Cotreatment with *Tridax procumbens* significantly restored the level of lipoproteins by decreasing the level of LDL, VLDL and increasing the HDL level.

Increased LDL and VLDL level may be due to elevated lipid biosynthesis by cardiac cyclic AMP. Higher levels of LDL has a positive correlation, where as high level of HDL has a negative correlation with myocardial necrosis (Buring *et al*., 1992). *Tridax procumbens* showed beneficial effect by reducing hyperlipidemia by suppressing cyclic AMP indicating the antihyperlipidemic effect of phytochemicals.

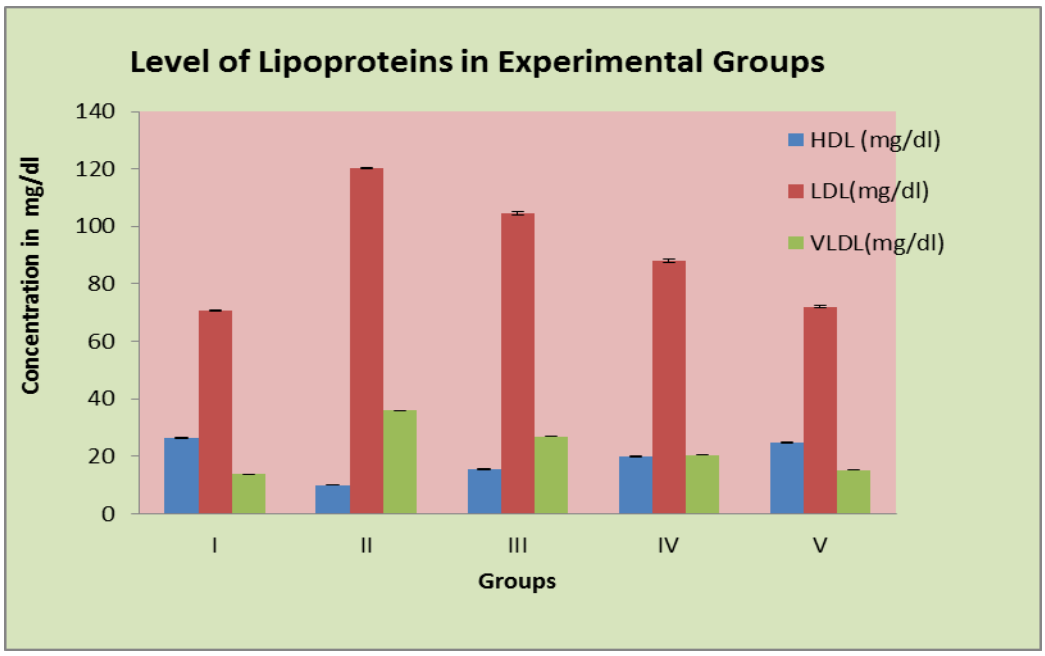

Figure I: Effect of Lipoproteins in different experimental groups.

Values are expressed as mean±SD for 6 rats in each group.

Statistically significant variations at P<0.05* group II vs group I, ** group III, IV, V vs group II.

Figure II depicted the levels of SOD, catalase, Glutathione peroxidase and glutathione reductase in the heart tissue of experimental animals. The level of antioxidants was found to be decreased in isoproterenol treated rats. The reduction in the level of antioxidants conferred

the production of oxidative stress. Oxidative stress due to the synthesis of free radicals inhibits the activity of antioxidants (Eshaghi *et al*., 2012). The rich antioxidants present in the plant extract in increasing concentration protected the myocardium from the free radicals and brought back the antioxidants to normal when compared to group II induced rats. Various studies have been reported that treatment with plants extracts increase the endogenous antioxidants in cardiovascular diseases (Mohanty *et al*., 2004).

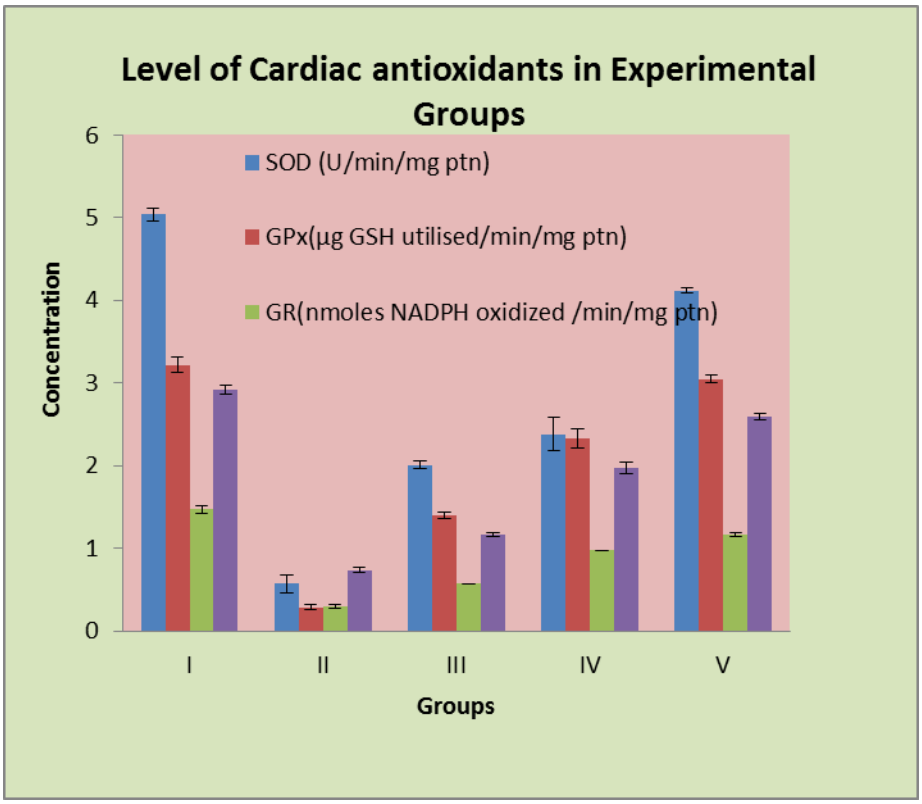

Figure II: Effect of antioxidants in different experimental groups.

Values are expressed as mean±SD for 6 rats in each group.

Statistically significant variations at $P<0.05^{*}$ group II vs group I, ** group III, IV, V vs group II.

CONCLUSION

In the present study, ethanolic extract of *Tridax procumbens* was administered to the experimental rats in different concentrations. The level of serum markers, lipid profile and lipoproteins were studied in serum and antioxidants were determined in heart tissue. The markers serve as a diagnostic index to study the extent of myocardial damage. Lipids play a prominent role in the development of atherosclerosis, and also in altering the structure of myocardium. Loss of antioxidant activities renders the heart tissue more susceptible to

oxidative damage. *Tridax procumbens* showed significant curative activity against myocardial damage in increasing concentration. Thus the ethanolic extract of *Tridax procumbens* can be used as an efficient drug for the treatment of myocardial infarction due to the presence of rich active constituents that play a defensive role.

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