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# **World Journal of Science and Research**



ISSN: 2455 2208

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Research Article Biochemistry

# PROTECTIVE EFFECT OF Vitis vinifera PEEL ON ISOPROTERENOL INDUCED MYOCARDIAL INFARCTION IN RATS.

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### ABSTRACT

This study aimed at *VitisVinefera* peel extract (VVPE) were pretreated against the isoproterenol induced myocardial infarction in Adult Albino Male rats and monitored the level of Serum of Cratine Kinase (CK), lactate dehydrogenase (LDH), Aspartate transaminase (AST or SGOT) and lipid peroxide (LPO). These are the diagnostic indicators of Myocardial infarction . Activities of Serum CK, LDH, SGOT and LPO were found to be increased in isoproterenol treated rats. Administration of VVPE to isoproterenol treated rats restored the elevated level of Serum and Myocardium. Glutathione (GSH) plays antioxidant defense process. Vitamin E and Vitamin C are antioxidant Vitamin. These level are decreased in Serum and Myocardium. In the present study VVPE pretreatment to Myocardial infracted rats restored the Serum levels of non-enzymic antioxidant Vitamin C and Vitamin E near to normal levels.

*Citation*: R.ShunmugaVadivu and G.Govindaraju (2016) Protective effect of *Vitis vinifera* peel on Isoproterenol induced Myocardial Infarction in rats. World Journal of Science and Research. 1 (2): 55-59.

#### Article Info:

Received on 10<sup>th</sup> August 2016 Accepted on 02<sup>nd</sup> Sept. 2016 Online September 2016

#### Keywords:

VitisVinefera peel Extract, Isoproterenol, Myocardial Infarction, Antioxidant, Glutathione.

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#### INTRODUCTION

Myocardial infarction (MI) one of the major causes of mortality is associated with ischemic necrosis of cardiac muscle due to compromised supply of blood to a portion of Myocardium for proper physiological function. (Anversa et al 1991). Most heart attacks are caused by the combination of the following: A Blood clot that blocks one of the Coronary arteris. Rupture of the unstable plague. (atherosclerosis). Endothelial dysfunction. Blockage of coronary artery deprives the heart muscle of blood and oxygen. If Blood flow is not restored within 20 to 40 minutes irreversible death of the heart muscle

will begin to occur. Muscles continue to die for 6-8 hours at which time the heart attack usually is "Complete". The dead heart muscle is replaced by scar tissue. Endothelial cells line the inner wall of coronary blood vessels, when these cells become disturbed (for eg. Eating high fat meal, sudden stress on high blood pressure) a piece of atherosclerotic plaque can dislodge and land in a narrow section of a coronary artery. High LDL (bad) cholesterol contribute to the development of plaque. When this happens blood flow is blocked and cause severe chest pain or even a heart attack(Anversa P 1991).

Endothelial dysfunction seems to be related to reduced levels of substance called Nitric Oxide. Normal level of nitric oxide help the coronary blood vessels relax and dilate. When these vessels are relaxed there is more blood flow to the heart.

Oxidative stress plays a role in cardiac and endothelial dysfunction. Increased oxidative stress represent a triggering mechanism for heart failure development &reduced the availability of the coronary blood vessels to relax. Therefore anti oxidants in the diet or possibly from supplements may improve the amount the function of nitric oxide. This is turn improved blood flow and reduced changes of heart attack. Isoproterenol is a βadrenergic agonist has been found to cause severe oxidative stress in the Myocardium through free radical formation. (Wexler&Greebery 1978). Animal studies have found that anthocyanidins (Crane berry, bilberry fruits) & other flavonoids including quercetin, resveratrol, and catechins (all found in high concentration in red wine) may strengthen blood vessels, improve circulation and prevent the oxidation of LDL (bad cholesterol) (chan et al., Biopharm (2000), In regard to human studies it has become evidence that biochemical markers of oxidative stress are markedly elevated in Heart failure patients (McMurray et al 1990) evidence of Increased oxidative stress by simple measurements in patient with detailed cardiomyopathy. In the present study, an attempt has been made to assess the protective effects of Vitis vinifera peel on cardiac function in isoproterenol-induced myocardial infarction in rats.

#### MATERIALS AND METHODS

## Animals

Adult Male albino Wister rats weighting 120-180 gm were obtained from the Indian Institute of Sciences, Bangalore. The Animals are housed in polypropylene cases and maintained in controlled temperature with standard rat chow food and water were provided alibitum.

#### **Chemicals:**

TBA, DNPH, Dipyridyl and reduced Glutathione purchased from Sigma Chemicals & all other reagents and chemicals used in this study were of analytical grade with high purity.

# Preparation of extract:-

Peel of vitisVinifera were collected. The peel were shade dried and extracted with Methanol (70%) used soxhlet extractor. A semisolid extract was obtained after complete elimination of methanol under

reduced pressure. The *VitisVinifera* peel extract was stored in refrigerator until used. The extract was dissolved in distilled water just before oral administration.

# **Experimental Design:-**

In this study Adult male albino Wistar rats were divided into the following groups. Group I: Normal Control Rats. Group II: Isoproterenol induced Rats (Received isoproterenol 20mg/100mg twice at an interval of 24 hr.). Group III: Isoproterenol induced + VVPE Treated rats (250mg/Kg body weight). After the experimental period the rats were killed by cervical decapitation. Blood was collected in a tube without anticoagulant from which serum was collected. Heart was dissected immediately washed in ice-cold saline and homogenate was prepared in 0.1M Tris-HCL buffer pH (7.4). The homogenate was centrifuged and the supernatant was used for the assay of Glutathione (GSH) and Lipid perioxide (LPO).

#### **Biochemical estimation**

The AST was estimated by the method of Reitman and frankel (1957). The activity of serum lactate dehydrogenase was measured by the method of kind (1959, 1965). The serum creatine phosphokinase was estimated Tanzar and Gilvarg (1959). A Thiobarbituric substances (TBA) was estimated by the method of Nichans and Samvelson, (1968). Total reduced glutathione was determined according to the method of Eliman (1959). Ascorbic acid level was estimated by the method of Roy and Kuether (1943). Serum a tocopherol was estimated by the method of Baker and Frank (1980).

#### RESULTS AND DISCUSSION

Several plants products are known to exhibit creditable ailments and need to be explored to identify their potential application and therapy of human ailments. (Nadkarni) In order to develop myocardial infaraction in rats, isoproterenol had been used in the present study. Isoproterenol induced myocardial infarction serves as a well standardized model to study the beneficial effect of many drugs and cardiac function. The pathological changes following isoproterenol administration are comparable to those of taking place in human myocardial infarction (Wexler, 1978).

Activities of Serum CK, LDH & SGOT were found to be increased in isoproterenol treated Group II rats when compared to normal control rats. An increase in the activity of these enzymes in serum is due to the leakage of enzymes from the heart as a

result of necrosis induced by isoproterenol. (Manjula*et al* 1992) In the present study near normal activity of the diagnostic marker enzymes in the serum of Group III animals showed significant cardio protective effect of VVPE Table1. Free radical generated by isoproterenol initiate lipid peroxidation of the membrane bound poly unsaturated fatty acids, leading to impairment of membrane structure and functional integrity. Levels of serum and myocardium lipid peroxide is represented in Table II. Administration of VVPE to isoproterenol treated rats restored the elevated level of lipid peroxide in serum and myocardium. This finding confirms the inhibitory effect of VVPE on lipid peroxidation.

GSH is the major non-protein thiol in living organism, which plays a central role in co-ordinating the body's antioxidant defense process. Isoproterenol GSH is the major non-protein thiol in living organism, which plays a central role in co-ordinating the body's antioxidant defense process. Isoproterenol treated rats shows a significant decrease in the

glutathione levels in serum and myocardium. Decreased glutathione levels in serum and myocardium may be due to its increased utilization in protecting "SH" containing protein from lipid peroxides. (ParithaIthayari and Shymala Devi, 1997) In the present study similar result was observed in isoproterenol induced rats pretreated with VVPE. (Fraster CR. Moukdar F., 2013).

Vitamin E and Vitamin C are antioxidant vitamin whose level was found to be significantly decreased in serum of isoproterenol rats. (Table IV). Vitamin E is thought to an important chain breaking antioxidant (Young IS, woods ide JV 2001) herbal showed cardio – production against isoproterenol induced Myocardial Infraction in rats (Prince SMP, S.Suman 2008). In the present study VVPE pretreatment to myocardial infracted rats restored the serum levels of non-enzymic antioxidant Vitamin E and Vitamin C near to normal levels.

Table :1 Activities of serum LDH, CK, SGOT (AST) are normal Control and Experimental rats

Groups	Particulars	Serum Myocardial Marker Enzymes		
		LDH IU/L	CK IU/L	SGOT IU/L
Groups I	Normal Control Rats	73.6 2 2.32	272.32 <u>+</u> 3.53	$23.37 \pm 0.58$
Groups II	Isoproterenol induced rats	157 ± 2.33*	533.59 <u>+</u> 5.06*	47.19 <u>+</u> 1.2*
Group III	Isoproterenol Induced + VVPE Treated Rats (250 mg/ksb.wt)	80.1 2 <u>+</u> 4.30 <sup>#</sup>	2.87.51 <u>+</u> 1.21 <sup>#</sup>	26.23 <u>+</u> 1.27 <sup>#</sup>

Values are expressed as Mean  $\pm$  SD for 6 animals in each group (students 't' test followed). P\*<0.001 significantly different from Group I P#<0.001 significantly different from Group II

Table :2 Levels of serum and Myocardium LPO in normal control and experimental rats.

Groups	Particulars	Serum LPO	Myocardium LPO
		(μ moles/litre)	(n moles / gm protein)
Group I	Normal Control Rats	2.42 <u>+</u> 0.16	3.12 ± 0.20
Group II	Isoproterenol Induced Rats	4.07 <u>+</u> 0.24*	5.61 ± 0.39*
Group III	Isoproterenol Induced + VVPE Treated Rats (250 mg/kg b.wt)	$2.53 \pm 0.06^{\sharp}$	$3.52 \pm 0.41^{\#}$

Values are expressed as Mean  $\pm$  SD for 6 animals in each group (students 't' test followed). P\*<0.001 significantly different from Group I P#<0.001 significantly different from Group II

Table :3 Levels of serum and myocardium reduced glutathione (GSH) in normal control rats and experimental rats

Groups	Particulars	Serum GSH (µ moles/litre)	Myocardium GSH (n moles / gm protein)
Group I	Normal Control Rats	2.64 ± 0.03	4.76 <u>+</u> 0.22
Group II	Isoproterenol Induced Rats	1.23 ± 0.04*	2.61 <u>+</u> 0.14*
Group III	Isoproterenol Induced + VVPE	$2.11 \pm 0.05^{\#}$	4.5 ± 0.21 <sup>#</sup>
	Treated Rats (250 mg/kg b.wt)		

Values are expressed as Mean  $\pm$  SD for 6 animals in each group (students 't' test followed). P\*<0.001 significantly different from Group I

P#<0.001 significantly different from Group II

Table :4 Levels of serum Vitamin E and Vitamin C in Normal control rats and experimental rats

Groups	Particulars	Vitamin E (mg/dl)	Vitamin C (mg/dl)
Group I	Normal Control Rats	12.30 <u>+</u> 0.43	2.15 <u>+</u> 0.11
Group II	Isoproterenol Induced Rats	9.20 <u>+</u> 0.27*	1.20 <u>+</u> 0.18*
Group III	Isoproterenol Induced + VVPE Treated	10.09 ± 0.31 <sup>#</sup>	$2.08 \pm 0.20^{\#}$
	Rats (250 mg/kg b.wt)		

Values are expressed as Mean  $\pm$  SD for 6 animals in each group (students 't' test followed).

P\*<0.001 significantly different from Group I

P#<0.001 significantly different from Group II

The present results clearly emphasize the beneficial action of as a cadioprotective agent. *Vitis vinifera* peel proved to be effective in reducing the extent of myocardial damage, associated lipid peroxidation, thus maintaining, as suggested by biochemical indices, the structure and function of the myocardium. The potential cardioprotective activity of *Vitis vinifera* may be due to the presence of therapeutic phytochemicalssuch as proanthocyanidins and natural polyphenolic.

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Source of support: Nil;

**Conflict of interest: None declared**