Research Article**Effect of *Foeniculum vulgare* Mill. on Isoproterenol induced myocardial infarction in albino rats****Natarajan P.*, Jasmine Grace**

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Abstract

Objective: The present study aimed to cardioprotective activity of hydroalcoholic extract of *Foeniculum vulgare* Mill. (HEFV) fruits on isoproterenol induced myocardial infarction in albino rats. **Materials and Methods:** Fruits of *Foeniculum vulgare* Mill. were air dried, coarsely powered and extracted with a mixture of alcohol and water (50:50,v/v) by a round bottom flask. The solvent was removed and dried crude extract was used for investigation. The animals were divided into 5 groups, Group I : Normal control (normal saline 10ml/kg p.o. for 30 days). Group II: Control (10ml/kg p.o. of normal saline for 28 days + Isoproterenol (ISO)-85mg/kg, s.c. on 29th and 30th day only). Group III: Hydroalcoholic extract of *Foeniculum vulgare* Mill-200mg/kg, p.o. for 30 days and ISO-85mg/kg, s.c. on 29th and 30th days only). Group IV: Hydroalcoholic extract of *Foeniculum vulgare* Mill-250mg/kg, p.o. for 30 days + ISO-85mg/kg, s.c. on 29th and 30th days only. Group V: Hydroalcoholic extract of *Foeniculum vulgare* Mill-400mg/kg, p.o. for 30 days + ISO-85mg/kg, s.c. on 29th and 30th days only). **Results:** The Hydroalcoholic extract of *Foeniculum vulgare* Millfruits at the dose of 200, 250 and 400mg/kg/p.o. respectively produce significant salvages the heart. **Conclusion:** In the current study, we found that HEFV protected myocardium from isoproterenol induced myocardial infarction and structural injury via normal levels of diagnostic marker enzymes and by restoring the glutathione and lipid peroxidation levels.

Keywords: Myocardial infarction, *Foeniculum vulgare* Mill, Isoproterenol, lipid peroxidation, glutathione

Introduction

Medicinal plants have been used by mankind from the beginning of human civilization for its therapeutic value (Toledo et al., 2010). Nature is being a source of medicinal agent for thousands of years and an impressive number of novel drugs have been secluded from natural sources, lots of these isolation was based on the uses of the agents in conservative medicine (Owolabi et al., 2007).

India is one of the world's 12 biodiversity centers with more than 45000 different plant species, among those, about 15000- 20000 plants have good medicinal value. Today, the herbal products indicate protection in difference to the synthetics that are regarded as hazardous to human and surroundings (Joy, 1998).

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Recently the use of herbs and herbal medicines in chronic diseases like MI (Myocardial infarction) is escalating in many parts of the world (Asdaq and Chakraborty, 2010).

Herbs and dietary supplements can have significant physiological effects (Adriane Fugh-Berman). In recent years, there has been a worldwide surge in the popularity of herbal/modern medicine, and presently there is enormous interest in rising new pharmaceutical products from such resources (Fahmy et al., 2010). Spices have played a vital role in the history of civilization, commerce and exploration as these had a universal approval as condiments and flavours in human diet as well as in treatment of ailments (Reddy et al., 2012).

Myocardial infarction, usually known as heart attack is a disease which occurs when the blood bring to a part of the heart is episodic, which causes death of heart tissue which means necrosis of a region of myocardium produce by an break in the blood supply to the heart commonly as a result of blockade of a coronary artery in addition called as cardiac infarction (Gurram et al., 2012).

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The present research was planned to evaluate the cardioprotective activity of *Foeniculum Vulgare* Mill. on experimental model of isoproterenol (ISO) induced myocardial infarction in albino rats.

Materials and methods

Taxonomical identification

The plant *Foeniculum vulgare* Mill. was authentically verified by Dr. J. Lohidas, Ph.D, Asst. Professor, Department of Botany and Research Centre, Scott Christian College, Nagercoil.

Extraction of plant material

Fruits of *Foeniculum vulgare* Mill were air dried, coarsely powered and extracted with a mixture of alcohol and water (50:50 v/v) by a round bottom flask. The solvent was removed and dried crude extract was used for investigation. Further, the extracts were subjected for the phytochemical study as well as pharmacological screening (Natarajan and Jasper, 2014).

Preliminary Phytochemical Analysis

The hydroalcoholic extract of *Foeniculum vulgare* Mill fruits were subjected to routine chemical analysis for the presence of various phytoconstituents (Khandelwal, 2006; Annes et al., 1997; Kokate, et al., 1984; Kokate et al., 1996).

Selection, housing and feeding condition of animals

Wister albino rats weighing between 150-200g were used in this experiment. The animals were housed 12 hours dark and 12 hours light at a temperature of (23±2°C) in polyethylene cages with Hindustan pellet diet and water *ad libitum*, and kept under controlled environment following the standard operating procedure of the animal house. The experimental design was approved by animal ethical committee (Reference number: 29/2013/IAEC/PRC) in Pankajakasthuri Research Centre, Kerala.

Experimental protocol

The animals were divided into 5 groups, each group comprising of six rats. The rats were grouped as follows:

Group I: Normal control (Received normal saline 10ml/kg p.o. for 30 days)

Group II: ISO Control (Received 10ml/kg p.o. of normal saline for 28 days +Isoproterenol-85mg/kg, s.c. on 29th and 30th day only).

Group III: Test rats (Received hydroalcoholic extract of *Foeniculum vulgare* Mill-200mg/kg, p.o. for 30 days + ISO-85mg/kg, s.c. on 29th and 30th days only).

Group IV: Test rats (Received hydroalcoholic extract of *Foeniculum vulgare* Mill-250mg/kg, p.o. for 30 days + ISO-85mg/kg, s.c. on 29th and 30th days only).

Group V : Test rats (Received hydroalcoholic extract of

Foeniculum vulgare Mill-400mg/kg, p.o. for 30 days + ISO-85mg/kg, s.c. on 29th and 30th days only) (Behera et al., 2012)

Isoproterenol induced myocardial infarction

After the drug treatment of animals for 28 days from group II to V according to the protocol, isoproterenol (85mg/kg b.w, s.c.) was dissolved in normal saline and administered subcutaneously for two consecutive doses at the interval of 24 hours. This dose is known to cause myocardial infarction in rats.

Collection and processing of blood for biochemical estimation

After 48 hours of the isoproterenol intoxication, animals were anaesthetized with ether and then the blood was collected by puncturing retro-orbital plexus and serum was analyzed for biochemical parameters using a semi auto analyzer. Then, the rats were sacrificed and the heart and liver was dissected out and homogenized. The tissues of heart and liver were analyzed for lipid peroxide and glutathione.

Preparation of tissue homogenate

The rats were sacrificed and the heart and liver was dissected out immediately and washed with chilled isotonic saline. The heart and liver tissue homogenates prepared in ice-cold 0.1 M Tris-HCl buffer, pH 7.2 were used for the determination of lipid peroxides and glutathione.

Results and discussion

The preliminary phytochemical investigation of the hydroalcoholic extract of *Foeniculum vulgare* Mill showed the presence of alkaloids, steroids, flavonoids, phenolic compounds, glycosides, proteins, saponins, tannins and terpenoids, oils, lignins, gums and mucillages. The results were shown in table 1.

Table1. Preliminary phytochemical screening of hydroalcoholic extract of *Foeniculum vulgare* Mill.

S. No.	Phytoconstituents	Hydroalcoholic extract
1.	Alkaloid	+
2	Carbohydrate	-
3	Glycosides	+
4	Tannins and phenols	+++
5	Gum and mucilage	+
6	Flavones and flavonoids	+++
7	Saponins	+
8	Steroids and sterols	+
9	Triterpinoids	++
10	Amino acids	+
11	Oils and Fat	+
12	Lignins	+

+ Presence, - absence, +++ High, ++ Moderate, + Medium

Table 2. Effect of hydroalcoholic extract of *Foeniculum vulgare* Mill on body weight of isoproterenol induced myocardial

Groups	Treatments	Initial body weight (g)	Final body weight (g)	% change of body weight
I	Normal Saline	180 ± 14	216± 17	↑ 20.33 %
II	Control (ISO only) 85mg/kg b.w, s.c.	185 ± 15	219.6± 18	↑ 18.46 %
III	HEFV (200mg/kg b.w, p.o.) + ISO (85mg/kg b.w, s.c.)	185 ± 9.5	227.5± 11	↑ 22.97 %
IV	HEFV (250mg/kg b.w, p.o.) + ISO (85mg/kg b.w, s.c.)	182.5 ± 6	227.5 ± 16	↑ 24.66 %
V	HEFV (400mg/kg b.w, p.o.) + ISO (85mg/kg b.w, s.c.)	180.8± 13.5	234 ± 22	↑ 29.49 %

Table 3. Effect of hydroalcoholic extract of *Foeniculum vulgare* Mill on cardiacmarker enzymes of isoproterenol induced myocardial infarction in albino rats

Groups	Treatments	LDH (IU/L)	CPK (IU/L)	SGOT (IU/L)
I	Normal Saline	185.33±9.81	88.33±5.85	60.33±4.36
II	Control (ISO only) (85mg/ kg b.w, s.c.	379.16±17.17***	396.7±14.65***	284 ±19.11***
III	HEFV (200mg/ kg p.o.) +ISO (85mg/ kg , s.c.)	287±26.55**	371.16±46.35	284±19.11
IV	HEFV (250mg/kg p.o.) + ISO (85mg/kg s.c.)	255.07±2.73***	276±44.4*	257.7±19.02*
V	HEFV (400mg/kgp.o.) + ISO (85mg/kgs.c.)	225..33±17.03***	167.9±35.5***	204.1 ± 6.5***

Value's were expressed as mean ± SD of six rats in each Group. Group II is compared with group I. Group III and IV, V are compared with Group II. P < 0.001***, P< 0.02**, P < 0.05 *, P values denotes significance

Table 4. Effect of hydroalcoholic extract of *Foeniculum vulgare* Mill on serum glucose and CRP Level of isoproterenol induced myocardial infarction in albino rats

Groups	Treatments	Glucose (mg/dl)	CRP (mg/dl)
I	Normal Saline	89.91±1.93	6.15±0.04
II	Control (ISO only) 85mg/kg b.w, s.c.	97.36±5.29	12.11±0.57***
III	HEFV (200mg/kgp.o.)+ ISO (85mg/kg s.c.)	89.83±3.06	9.97±1.79
IV	HEFV (250mg/kgp.o.)+ ISO (85mg/kg s.c.)	85.53±4.81	9.85±2.54
V	HEFV (400mg/kg p.o.) + ISO (85mg/kg s.c.)	78.83±5.19**	5.18±0.81***

Value's were expressed as mean ± SD of six rats in each group.Group II is compared with group I. Group III and IV, V are compared with Group II. P < 0.001 ***,P< 0.02 **, P < 0.05*, P values denotes significance.

Data (table 2) represent the body weight of the experimental rats. The percentage increase in the body weight of the untreated (normal) rats was found to be 20.33. In the control group where only isoproterenol was administered, the body weight increased by the percentage of 18.46. The body weight of drug treated rats (groups III, IV & V) was increased by 22.97, 24.66 and 29.49 percentage respectively.

Biochemical test was performed to estimate the effect on cardiac marker enzymes of FVHE on ISO induced myocardial infarction in albino rat. An increased level of SGOT, LDH and CPK was observed in the isoproterenol administered rats when compared

to the normal rats. Pretreatment with hydroalcoholic extract of *Foeniculum vulgare* at all the three doses significantly decreased the levels of SGOT, LDH and CPK when compared with isoproterenol treated rats. The results were shown in table 3.

Effect of *Foeniculum vulgare* Mill. on serum glucose and CRP of isoproterenol induced myocardial infarction in albino rats. The levels of serum glucose and CRP were significantly decreased in the drug extract treated rats, when compared to isoproterenol treated group. The results were shown in the table 4.

Table 5. Effect of hydroalcoholic extract of *Foeniculum vulgare* Mill on lipid profile of isoproterenol induced myocardial infarction in albino rats

Groups	Treatments	Triglycerides (mg%)	Total Cholesterol (mg %)	LDL (mg %)	HDL (mg%)	LDL/ HDL Ratio
I	Normal Saline	89.5 ±6.5	79.8±6.4	39.2±3.74	22.7±4.9	1.72±0.1
II	Control (ISO only) 85mg/kg s.c.	145.3±4.17***	117.8±11.4**	58.5±14.5	30.4 ±10.4	1.9±0.05
III	HEFV (200mg/kg p.o.) + ISO (85mg/Kg s.c.)	129.6±9.5	100.9±7.9	48.6±7	26.3 ±4.4	1.85 ±0.16
IV	HEFV (250mg/kg p.o.) + ISO (85mg/kg s.c.)	115.6±9.7**	91.6±6.41	41.8±8.8	27.4 ±3.78	1.52 ±0.12
V	HEFV (400mg/kg p.o.) + ISO (85mg/kg s.c.)	97.25±2.89***	81.6±11.39**	32.6±5.6	29.6±5.46	1.1±0.7

Value's were expressed as mean ± SD of six rats in each group. Group II is compared with group I. Group III and IV, V are compared with Group II. P<0.001***, P<0.02**, P<0.05*, P values denotes significance

Table 6. Effect of hydroalcoholic extract of *Foeniculum vulgare* Mill on Renal function test of isoproterenol induced myocardial infarction in rats

Groups	Treatments	Urea (mg/dl)	Creatinine (mg/dl)	Uric acid (mg/dl)
I	Normal Saline	34.66±6.71	0.86±0.15	3.68±0.51
II	Control (ISO only) 85mg/kg b.w, s.c.	38.16±4.40	1.01±0.13	4.94±0.30
III	HEFV (200mg/kg p.o.) + ISO (85mg/kg s.c.)	29.58±3.18	0.17±0.15	4.28±0.66
IV	HEFV (250mg/kg p.o.) + ISO (85mg/kg s.c.)	33.21±7.56	0.96±0.08	4.56±0.52
V	HEFV (400mg/kg p.o.) + ISO (85mg/kg s.c.)	28.83±6.79	0.66±0.22	4.53±0.73

Value's were expressed as mean ± standard deviation (SD) of six rats in each group. Group II was compared with group I. Group III and IV, V were compared with Group II. P < 0.001***, P < 0.02**, P < 0.05*, P values denotes significance.

Table 7. Effect of hydroalcoholic extract of *Foeniculum vulgare* Mill on liver function test of isoproterenol induced myocardial infarction in albino rats

Groups	Treatments	Bilirubin (mg%)	SGPT (IU/L)	ALP (IU/L)	Total protein (g%)	Albumin (g%)	Globulin S (g%)
I	Normal Saline	0.8±0.42	76.86±8.59	133.83±8.58	5.76±1.06	3.11±0.46	2.65±1.18
II	Control (ISO only) 85mg/kgs.c.	1±0.16	136±50.59	184.16±27.08	5.78±1.31	3.46±0.34	2.32±1.33
III	HEFV (200mg/kg p.o.) +ISO 85mg/kgs.c.)	0.50±0.16	125.16±6.99	183.1± 5.40	5.23±0.35	3.04±0.19	2.18±0.49
IV	HEFV (250mg/kg p.o.) +ISO 85mg/ Kg s.c.)	0.60±0.11	130.35±1.82	129.53±14.84	5.15±0.95	3.9±0.56	1.25±1.09
V	HEFV (400mg/kg p.o.) + ISO 85mg/kg s.c.)	0.65±0.03	99.25±13.04	122.8±6.57	4.9±0.74	3.53±0.65	1.37±0.83

Value's were expressed as mean ± SD of six rats in each group. Group II was compared with group I. Group III and IV, V were compared with Group II.

Effect of *Foeniculum vulgare* Mill. on lipid profile of isoproterenol induced myocardial infarction in albino rats. The levels of triglycerides, total cholesterol and LDL cholesterol were increased in the isoproterenol treated group and ratio of LDL to HDL cholesterol also increased whereas, the triglycerides level decreased significantly in the IV and V groups of drug treatment. The total cholesterol level was also decreased significantly in V group. In the drug treatment group the LDL

cholesterol was decreased than the control group and the HDL cholesterol was increased progressively. The LDL/HDL ratio is decreased than the control group. The results were shown in the table 5.

Effect of *Foeniculum vulgare* Mill on renal function test of isoproterenol induced myocardial infarction in albino rats. There is no significant difference in urea, creatinine and uric

Table 8. Effect of hydroalcoholic extract of *Foeniculum vulgare* Mill. on liver and heart lipid peroxides of the isoproterenol induced myocardial infarction in albino rats

Groups	Treatment	Liver	Heart
		Lipid peroxide level (mM/100 g of wet tissue)	Lipid peroxide level (mM/100 g of wet tissue)
I	Normal Saline	0.99±0.12	1.10±0.01
II	Control (ISO only) 85mg/kg b.w, s.c.	1.93±0.1***	4.2± 0.06***
III	HEFV (200mg/kg b.w, p.o.) + ISO (85mg/kg b.w, s.c.)	1.26± 0.05***	3.1±0.27**
IV	HEFV (250mg/kg b.w, p.o.) + ISO (85mg/kg b.w, s.c.)	1.23±0.02***	2.76±0.02***
V	HEFV (400mg/kg b.w, p.o.) + ISO (85mg/kg b.w, s.c.)	1.11±0.03***	1.23±0.02***

Value's were expressed as mean ± SD of six rats in each group. Group II was compared with group I. Group III and IV, V were compared with Group II. P <0.001***, P<0.02**, P<0.05*, P values denotes significance

Table 9. Effect of hydroalcoholic extract of *Foeniculum vulgare* Mill on liver and heart glutathione of isoproterenol induced myocardial infarction in albino rats

Groups	Treatments	Liver	Heart
		Glutathione level (mg/100g of wet tissue)	Glutathione level (mg/100g of wet tissue)
I	Normal Saline	95.15± 4.30	157± 6.02
II	Control (ISOonly) 85mg/kg s.c.	63.21±6***	92.34± 3.2***
III	HEFV (200mg/kg p.o.) + ISO (85mg/kg s.c.)	156.7± 29.59**	177.4± 27.03**
IV	HEFV (250mg/kg p.o.) + ISO (85mg/kg s.c.)	191.68± 3.9***	204± 3.6***
V	HEFV (400mg/kg p.o.) + ISO (85mg/kg s.c.)	211.8± 3.06***	226.1± 4.9***

Value's were expressed as mean ± SD of six rats in each group. Group II is compared with group I. Group III and IV, V are compared with Group II. P <0.001***, P<0.02**, P<0.05*, P values denotes significance.

acid were noted in all the groups of experimental rats (table 6).

Effect of *Foeniculum vulgare* Mill on liver function test of isoproterenol induced myocardial infarction in albino rats. The levels of SGPT, Bilirubin and ALP were increased in the isoproterenol treated group, when compared to normal group. Pretreatment of the drug extract in all the three doses showed decreased level of SGPT and ALP. The levels of bilirubin, total protein, albumin and globulin did not differ in the experimental groups of rats (table 7).

The lipid peroxide levels in the liver and heart tissue homogenate of isoproterenol treated rats were significantly increased, when compared to the normal rats. Pretreatment with drug at all the three doses caused a significant decrease in level of lipid peroxide in both heart and liver tissue, when compared to group 2. The results were show in table 8.

The level of glutathione in the heart and liver tissue homogenate of isoproterenol treated rats were significantly decreased, when compared to the normal rats. Pretreatment with drug at all the three doses caused a significant increased in level of glutathione in both heart and liver tissue (table 9).

Summary and conclusion

The study was conducted by administrating three different doses of HEFV (200mg/kg, 250mg/kg, 400mg/kg p.o. respectively) for 30 days in albino rats. The serum was collected and analyzed for various biochemical parameters such as SGOT, CPK, CRP, LDH, Urea, creatinine, blood sugar, liver function test, lipid profile test and levels of glutathione and lipid peroxide in liver and heart tissue.

The level of diagnostic marker enzymes such as SGOT, CPK, LDH, TG, TC were increased in ISO control group whereas

Figure 1. The representative photographs of H & E (hematoxylin and eosin, 400×). Stained rat heart sections: Group-I: The heart sections obtained from normal control; Group-II: Showing severe necrotic changes of karyolysis and disappearance of group of myocytes; Group-III: Showing mild necrosis; Group-IV: Showing slight regeneration of myocardial cells; Group-V: Remarkable regeneration of myocardial cells

significantly decreased in the drug (HEFV) treated rats. Hence, it prevent the leakage enzyme from the heart.

The level of serum glucose and CRP were increased in the control group whereas the drug (HEFV) treated groups level of serum glucose and CRP were significantly decreased. This shows the HEFV possess hypoglycemic activity and reduces inflammation.

The level of lipid peroxide in the liver and heart tissue were increased in the control rats. The level of above parameter was decreased in HEFV treated group. This shows HEFV exhibited antioxidant property. No significant change in renal and liver function test was observed in the group of control and drug treated rats. This indicates drug is non - toxic to kidney and liver.

The isoproterenol treated control group showing moderate to severe histological changes, while in the drug (HEFV) treated group there was remarkable improvement in sections of heart architecture.

The above mentioned all findings summarises the present study suggests that administration of *Foeniculum vulgare* Mill may prove to be a potential therapy to treat myocardial infarction.

In conclusion, the present study showed that acute ISO injection in experimental animals induces MI which was confirmed by biochemical changes and histopathological studies. Pretreatment with *Foeniculum vulgare* Mill prevents the cellular damage and remarkable protection over ISO induced changes in marker

enzyme activity by the virtue of its potent antioxidant activity. These findings might be helpful to understand the beneficial effects of *Foeniculum vulgare* Mill against ISO induced MI. Eventhough, further study will be in progress at department of the pharmacology and toxicology, S.B College of pharmacy, Sivakasi to confirm its exact mechanism.

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Conflicts of interest: Not declared.

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