CARDIOPROTECTIVE EFFECT OF *ocimum basilicum* SEEDS OIL AND *inum usitatissimum* SEEDS OIL ON PHYSIOLOGICAL PARAMETERS AND HISTOPATHOLOGICAL CHANGING AGAINST ISOPROTERENOL INDUCED ACUTE MYOCARDIAL INFARCTION IN MALE RABBITS

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ABSTRACT

The current study was undertaken to investigate the possible protective effect of *Ocimum basilicum* seeds oil and *Linum usitatissimum* seeds oil on some physiological parameter and histopathological changes when induced acute myocardial infarction in rabbits by isoproterenol.Thirty-six male rabbits were divided into six groups: group (C): control negative,group (ISO): received isoproterenol (control positive), (BP) group: basil seed oil protective group, (FP) group: flaxseed oilprotective group, (BT) group: basil seed oil treated group and (FT)group: flax seed oil treated group. The results showed thata significant decrease in the biomarker enzymes(CK-MB, LDH, AST, ALT and ALP) concentration and serum MDA in the BP, FP, BT, and FT groups compare with ISO group. In addition to that, the basil oil and flaxseed oil protect and improvement histopathological findings in the myocardium tissue of isoproterenol effect.

INTRODUCTION

Acute myocardial infarction (AMI) is a serious ischemic heart disease leading to worldwide morbidity and mortality. Myocardial infarction occurs as a result of an imbalance between coronary blood supply and myocardial demand(1). It is well known that ischemic tissue generates oxygen-derived free radicals and other reactive species

which cause oxidative damage of membrane proteins, lipids and carbohydrates leading to qualitative and quantitative alterations of the myocardium (2). Isoprenaline (Isoproterenol) is a synthetic catecholamine and β-adrenergic agonist that induces severe stress in the myocardium when injected subcutaneously in a large dose resulting inthe pathophysiological changes in the heart muscle of the experimental animal, similar to the myocardial infarction in human (3,4).

Ocimum basilicum (basil) a member of *Lamiaceae* family originated in Asia and Africa. The different parts of the basil have been widely used in traditional medicine to treat a wide range of diseases. Scientific studies have recognized that compounds in basil oil have strong antioxidant, anticancer, antiviral, antimicrobial properties prevention and treatment of cardiovascular disease(5,6).

Linum usitatissimum (flax) a member of *linaceae* family, it was used in ancient Egypt and Greece for medical purposes. In the last two decades, flaxseed has been the focus of increased attention in the field of diet and disease research due to the possible health benefits associated with some of its biologically active components, such as oil, flax lignans and fibers in reduction of cardiovascular disease, atherosclerosis, diabetes, cancer, arthritis, autoimmune and neurological disorders (7,8).This work amid to determine the effect of protective and ameliorative effect of *Ocimum basilicum* seeds oil and *Linum usitatissimum* seeds oil on physiological parameters and histopathological changing in acute myocardial infarction in male rabbits induced by isoproterenol.

MATERIALS AND METHODS

` Thirty-six healthy male domestic rabbits brought from local market /Basrah, weighting (1200-1750) grams. The rabbits kept under observation for 10 days. They were provided with feed and tap water *adlibitum*.Then rabbits were randomly divided into six groups (6 rabbits for each group):Group C:negative control received 1ml olive oil orally for 32 days. Group ISO: Positive control received isoproterenol (70mg/kg S.C.) for 2 consecutive days. Group BP:Received 900 mg/Kg basil oil orally for 32 days.Then, on

day 31 isoproterenol (70mg/kg S.C.) for 2 consecutive days.Group FP: Received 50 mg/Kg flaxseed oil orally for 32 days. Then, on day 31, isoproterenol (70mg/kg S.C.) for 2 consecutive days.Group BT: Received isoproterenol (70mg/kg S.C.) for two consecutive days then, received 900 mg/Kg basil oil orally for 32 days. Group FT: Received isoproterenol (70mg/kg S.C.) for two consecutive days then, received 50mg/Kg flaxseed oil orally for 32 days.

Blood collection: At end of the experiment the blood samples were collected from ear margin vein by using butterfly needles (23 G).Blood sample then was centrifuged to isolate blood serum to estimate the biochemical measurement.

Biochemical assay: The serum creatine kinase-myocardial band (CK-MB) and lactate dehydrogenase (LDH) determination by using commercial kits(Human/Germany).While

the serum enzymes alanine aminotransferase (ALT),as part at aminotransferase. Serum malodialdehyde (MDA) was determined by colorimetric method according to (9).

Histological preparation: At the end of experiment, the heart samples removed and fixed in 10% buffered formalin, dehydrated progressively in increased ethanol concentrations, treated with xylene and embedded in paraffin. Five-micron thickness sections cutting routinely prepared using a microtome. Then, tissue section was mounted on glass slides and stained with Hematoxylin and Eosin stain (10).

Statistical analysis of data was performed on the basis of Two-Way Analysis of Variance (ANOVA) by using computerized SPSS program version 22.0.The data were presented as mean ± stander deviation. Lest significant different test (LSD) was calculated to test difference between means (groups)(11).

RESULTS

The current study revealed a significant decrease($P<0.05$) in serum CK-MB concentration in the BP and FP group treated with basil oil and flaxseed oil as compared with ISO group. Whereas, CK-MB concentrations revealed a significant decrease ($P<0.05$) in BT and FT group compared with ISO group (Table-1).

Table (1): Effect of Basil Oil and Flaxseed Oil Extract on Serum CK-MB Concentration on Isoproterenol Induced Acute Myocardial Infarction in Male Rabbits.

Parameter	Treatment groups					
	C	ISO	BP	FP	BT	FT
CK-MB U/L	15.93 ±4.23 B	84.34 ±8.91 A	28.54 ±7.99 B	29.51 ±7.20 B	25.09 ±9.22 B	27.48 ±5.14 B

Values express as mean ± SD., n = 6/group. Capital letters denote difference between groups P<0.05. C: control group, ISO: isoproterenol, BP: basil oil, FP: flaxseed oil for 30 days then received isoproterenol, BT: AMI animals received basil oil, FT: AMI (Acute myocardial Infarction) animals received flaxseed oil. Zero day: after AMI induction in ISO, BT, and FT group.

There was a significant decrease (P<0.05) in serum LDH and ALT concentration in BP,FP, BT,and FTgroups at day 33 compared with ISO group but it is still significantly higher than control value except AST value in FT group(Table-2).

The present study demonstrated that there was a significant decrease (P<0.05)on ALT and ALP concentration in BP and FB group treated with basil oil and flaxseed oil respectively after isoproterenol injection compared with ISO group.The results also indicated that oral administration of basil oil and flaxseed oil to the AMI rabbits in BT and FT group causes a significant decreased (p<0.05) in serum ALT and ALP concentration when compared with ISO group Besides, there was no significant differences between FT and control (Table-2).

Table (2):Effect of Basil Oil and Flaxseed Oil Extract on Serum LDH,AST, ALT, and ALP concentration on Isoproterenol-Induced Acute Myocardial Infarction in Male Rabbits

parameter Group	LDH U/L	AST U/L	ALT U/L	ALP U/L
C	196.9 ±21.9 D	11.39 ±2.26 D	7.00 ±1.41 B	11.44 ±1.62 C
ISO	509.1 ±28. 2 A	34.54 ±3.28 A	20.66 ±1.7 A	25.61 ±2.91 A
BP	229.4 ±19.5 B	20.64 ±3.89 B	9.00 ±21.5 B	16.39 ±2.1 B
FP	259.7 ±21.8 B	20.86 ±5.52 B	9.00 ±2.82 B	14.18 ±1.29 C
BT	267.2 ±18.9 BC	16.39 ±2.76 C	10.50 ±2.42 B	14.89 ±0.99 B
FT	244.9 ±14.3 C	14.88 ±4.45 D	7.16 ±1.4 B	13.99 ±0.49 C

Values express as mean ± SD., n = 6/group. Capital letters denote difference between groups P<0.05. C: control group, ISO: isoproterenol, BP: basil oil, FP: flaxseed oil for 30 days then received isoproterenol, BT: AMI animals received basil oil, FT: AMI (Acute myocardial Infarction) animals received flaxseed oil. Zero day: after AMI induction in ISO, BT, and FT group.

The mean value of serum MDA concentration of BP and FP group treated with basil oil and flaxseed oil revealed that statistical differences were absent between these groups and control. While, there was significant decrease (P<0.05)in serum MDA concentration in BP and FP group compared with ISO group.

The result also revealed that treatment of AMI rabbits with basil oil and flaxseed oil extract showed a significant decrease (P<0.05)in serum MD a concentration in BT and FT group compared with ISO group and the values of these group reach to control (Table-3).

Table (3): Effect of Basil Oil and Flaxseed Oil Extract on Serum MDA Concentration on Isoproterenol-Induced Acute Myocardial Infarction in Male Rabbits

Parameter	Treatment					
	C	ISO	BP	FP	BT	FT
MDA U/L	0.47 ±0.03 B	3.99 ±0.68 A	0.45 ±0.05 B	0.47 ±0.05 B	0.48 ±0.9 B	0.46 ±0.07 B

Values express as mean ± SD., n = 6/group. Capital letters denote difference between groups P<0.05. Small letters denote difference within groups P<0.05. C: control group, ISO: isoproterenol, BP: basil oil, FP: flaxseed oil for 30 days then received isoproterenol, BT: AMI animals received basil oil, FT: AMI (Acute myocardial Infarction) animals received flaxseed oil. Zero day: after AMI induction in ISO, BT, and FT group.

The histological sections of heart tissue of normal control rabbits revealed normal myocardial cells.The myocardial fibers were arranged regularly with plain striations connected by intercalated discs(Figure-1).Sections of isoproterenol treated heart rabbits (ISO group)showed degenerated and vacuolated of myocardial cells, congested of blood vessels, hemorrhage between the myocardial muscle fibers and associated with adipose tissue (fat cells) in pericardial(Figure-2). Whereas, rabbits treated with basil oil then injected with isoproterenol (BP) group showed normal myocardial cells and large pericardial area of adipose tissue (Figure-3). In addition, same changes occur in rabbits treated with flaxseed oil then injected with isoproterenol (FP) group (Figure-4).

Microscopically cellular changes of AMI rabbits treated with basil oil (BT) group was degenerated, vacuolated myocardial muscle cells in the left ventricle and large pericardial

areas of adipose tissue(Figure-5).While AMI rabbits treated with flaxseed oil (FT) group showed normal myocardial muscle cells in left ventricle and pericardial area of adipose tissue(Figure-6).

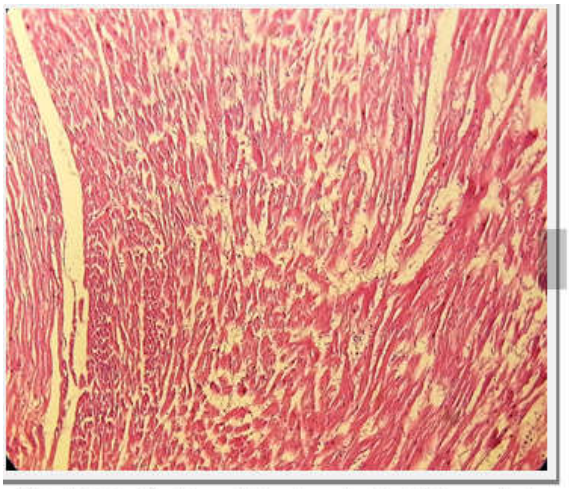

Fig. (4-1): -Section of the heart of rabbit control. Showing an areas of heart normal myocardial cells in left ventricle). Stained with H&E,400X.

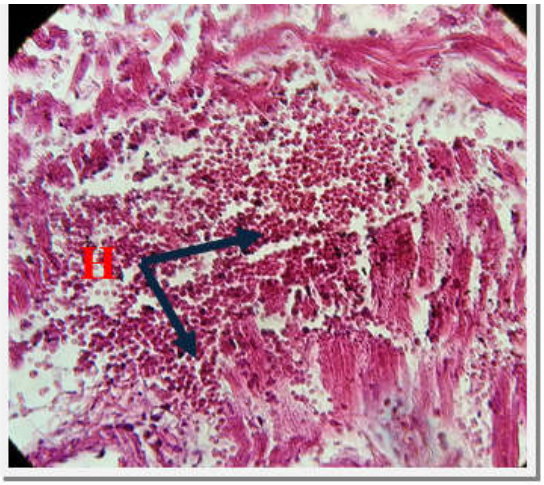

Fig. (4-2): - Section of the heart of rabbit treated with ISO. Showing an areas of degenerates vacuolated myocardial cells in left ventricle, associated with congestion and hemorrhage (H) also pericardial areas of adipose tissue (fat cells). Stained with H&E,400X.

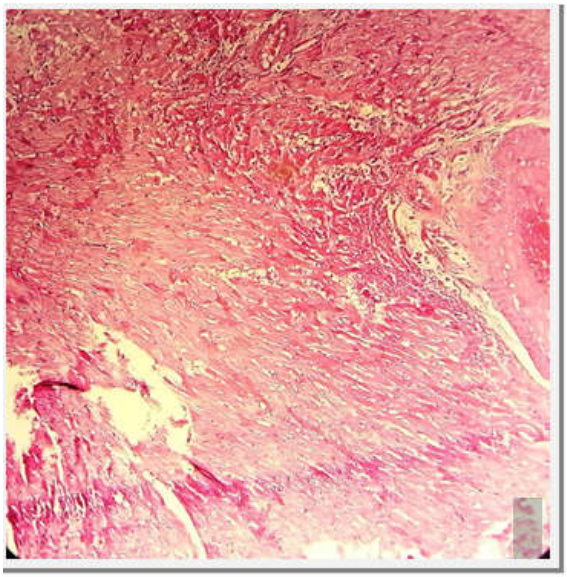

Fig. (4-3): -Section of the heart of rabbit treated Basil oil + ISO. Showing an areas of heart normal myocardial cells in left ventricle and large pericardial area of adipose tissue. Stained with H&E.100X.

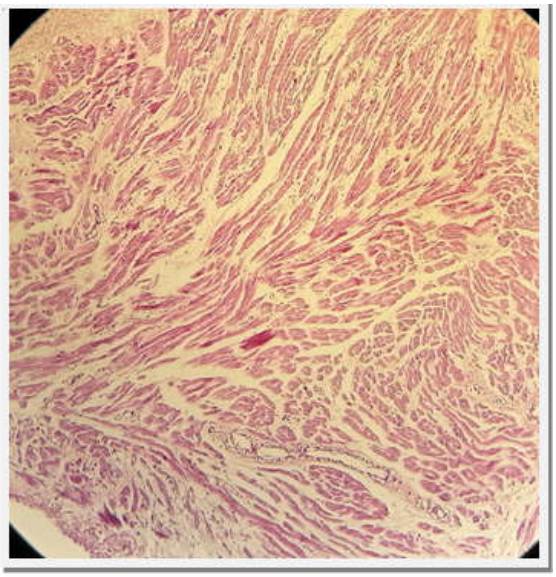

Fig. (4-4): -Section of the heart of rabbit treated Flax seed oil + ISO. Showing an areas of heart normal myocardial cells in left ventricle and large pericardial area of adipose tissue. Stained with H&E.100X

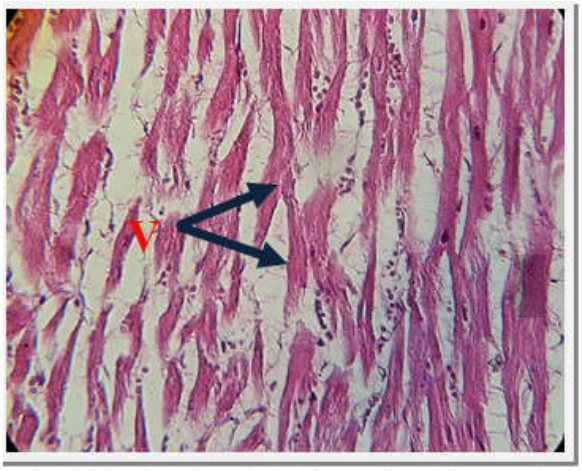

Fig. (4-5): -Section of the heart of rabbit treated with ISO+ Basil oil. Showing an areas of heart degenerate vacuolated (V) myocardial cells (in ventricle), also large pericardial areas of adipose tissue. Stained with H&E,400X.

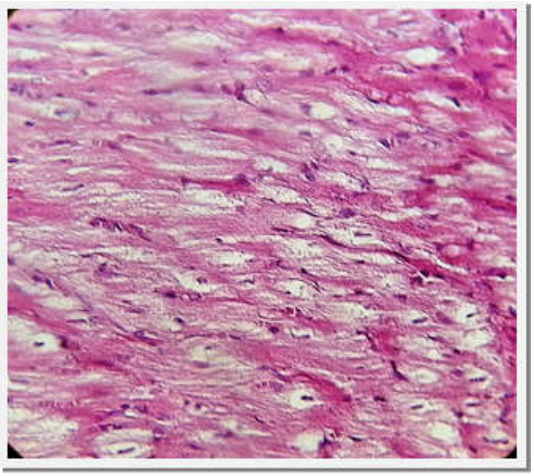

Fig. (4-6): -Section of the heart of rabbit treated with ISO+ Flax seed oil. Showing an areas of heart normal myocardial cells in left ventricle and pericardial area of adipose tissue. Stained with H&E,100X

DISCUSSION

The obtained results revealed a significant reduction in theCK-MB, LDH, AST, ALT and ALP concentration in the acute myocardial infarction rabbits treated with basil oil and flaxseed oil respectively and in basil oil+isoproterenol (BP group) and flaxseed oil +isoproterenol (FP group). The injection with a high dose of isoproterenol increased thelevel of these enzymes due to their leakage from the damaged heart tissues into the blood stream through myocardial necrosis because to myofibril degeneration and myocyte necrosis (6).These cellular enzymes are released for a response to β-adrenergic stimulation or because of the changes in the integrity and permeability plasma membrane. The changes maybe damage the sarcolemma caused by the isoprenaline(12).Treatment of different groups of rabbits with basil oil and flaxseed oil significantly reduced the isoproterenol-induced secretion of all cardiac diagnostic marker enzymes. This decreased level or reduction inthe secretion of enzymes could be repairing and maintenance of the membrane of the myocardial cell and provide cardiomyocytes less leaky attributed to stabilization of myocyte membranes resultant to inhibition of lipid peroxidation and membrane disruption.

This finding is in agreement with previous study (13) who found that linseed oil pre-treatment prevented approximately all the parameters isoproterenol-induced myocardial infarction in rats.In addition, flaxseed oil has a significant protective effect on the heart against isoproterenol-induced myocardial infarction due to a beneficial effect of the important fraction of ALA. Other research demonstrated that rosmarinic acid in *Ocimum basilicum* prevented LDH level elevation in rats probably by suppressing oxidative stress and consequent myocardial necrosis (14).

As basil oil and flax seed oil are essential oil and rich in omega fatty acids, so our results agree with another authors studied the cardio protective effect of omega fatty acids. (15)have shown that pretreatmentomega-3 PUFA could significantly decrease CK-MB elevation after per coetaneous coronary intervention (PCI) andomega-3 PUFA may have a protective effect against post-PCI cardiovascular events. This finding might be due to anti-platelet and anti-inflammatory effects of omega-3 PUFA, because both platelet aggregation and inflammation play an important role in the pathogenesis of atherosclerosis.

The acute phase of myocardial necrosis induced by isoproterenol has been associated with a generation of highly cytotoxic reactive oxygen. Therefore, the interaction of free radicals with cellular elements like lipids, form oxidative products such as lipid peroxides inside the infracted myocardium. These products later decompose toa number of final products such as malodialdehyde, the measurement of MDA an indicator of lipid peroxidation level and free radical activity in serum and myocardium (14,16).The finding indicated to significant increase in serum MDA level in all groups treated with basil oil and flaxseed oil compared with ISO group (Table-4). This finding may be due to the presence of omega PUFA, which acts as the antioxidant agent and neutralizing free radicals(17,18,19).The present study is in agreement with (20) who reported that oral administration of basil oil was able to improve and restore the level of endogenous antioxidants and decrease MDA level in the serum compared to MI rats.The decrease in MDA in the serum when given flaxseed oil orally to rats induced oxidative stress(21). The antioxidant activity of flaxseed oil may be attributed to its high content of omega-3

PUFA which inhibit oxygen radical production by white blood cells and improves cardiovascular health due to its powerful antioxidant activity.

Our results indicate that treatment of the AMI rabbits, pretreated with basil oil and flaxseed oil markedly preventing and ameliorate the alteration in heart pathology due to isoproterenol injection with tendency to return to their normal texture. This profile is consistent with other studies(20,22). Isoproterenol generates free radicals leading to lipid peroxidation. Mitochondrial membrane contains a large amount of PUFA in its phospholipids that are highly susceptible to lipid peroxidation, an important impairment in biological membrane. A high levels of lipid peroxidation in heart mitochondrial may decrease mitochondrial membrane fluidity, increase negative surface charge distribution and alter membrane ionic permeability (23).Therefore, accelerated lipid peroxidation cause severe stress lead to damage of the myocardium resulting in infarct area like necrosis(24,25).

Anew study in 2014 (20)showed that a basil oil markedly reduced the epinephrine induced myocardial cellular changes and near normal morphology of cardiac muscle, this promoted the cardio protective action of the basil oil. The protective property of basil oil against myocardial injury may be indicated to its anti-inflammatory property which diminishes formation, release, and activity of inflammatory mediators as histamine,cytokines, leukotrienes, and prostaglandins (26).

Antioxidant defenses enablethe system to eliminate ROS, return the prevailing reducing environment and repair the tissue damage (27).In addition, pretreatment with alpha linolenic acid (ALA) was reported to protect against myocardial cell apoptosis by inhibition of ROS generation, consequently contributing to reducing myocardial infarction size (28).While,(29) suggests that linalool can exert its action to protect the myocardial damage by limiting the generation of free radicals which can prevent the necrosis of the tissue and might be restored activity of the tissue.Also, flaxseed oil seem to accelerate repair and regeneration of injured organelles such as mitochondria and lysosomes, plasma membrane by activating endogenous antioxidant defense mechanism (30).

Conclusion: Biochemical and histological findings of the present study indicate that basil seed oil and flaxseed oil have antioxidant properties in myocardium and protect against isoproterenol induced oxidative stress and myocardial infarction.

دراسة التأثير الوقائي لعضلة القلب للمستخلص الزيتي لبذور نبات الريحان وبذور نبات الكتان على المعاييرالفسلجية والنسجية لذكور الأرانب المصابة بأحتشاء القلب الحاد المستحدث بواسطة الايزوبريتنول

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الخلاصة

اجريت الدراسة الحالية لمعرفة احتمالية التأثير الوقائي لزيت بذور الريحان والكتان على بعض المعايير الفسلجية والنسجية للأرانب المصابة بأحتشاء القلب الحاد المستحدث بواسطة الايزوبريتنول. قسمت ستة ثلاثون ذكر أرنب الى ستة مجاميع متساوية .مجموعة (c): السيطرة السالبة ومجموعة (ISO):السيطرة الموجبة حقنت ايزوبريترنول ومجموعة (BP): زيت بذور الريحان الوقائي ومجموعة (FP): زيت بذور الكتان الوقائي ومجموعة (BT):زيت بذور الريحان العلاجي و ومجموعة (FT): زيت بذور الكتان العلاجي. وقد اظهرت النتائج انحفاضا" معنويا" في تراكيز انزيمات علامات القلب (CK-MB, LDH, AST, ALT and ALP) ومصل MDAفي كل من المجاميع التالية BP وFP و BT وFT بلاضافة الى ان زيت كل من بذور الريحان والكتان له تأثير وقائي ومحسن على نسيج عضلة القلب من تأثير الايزوبريتنول.

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