Original Article

The effect of dipeptidyl peptidase-4 inhibitors or curcumin on diet induced metabolic syndrome with cardiac dysfunction in rats

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ABSTRACT

Background: Metabolic syndrome (MS) increases the risk of developing cardiovascular diseases (CVDs) which are the leading cause of death worldwide.

Objective: This study is aiming to investigate the curative effects of dipeptidyl peptidase-4 inhibitors and the prophylactic effects of curcumin on diet induced metabolic syndrome which is associated with cardiac dysfunction in rats.

Methodology: sixty adult male albino rats were divided into six groups: Group I: (control). Group II: (MS induced). Group III: (Vildagliptin only). Group IV: (Curcumin only). Group V (therapeutic): Vildagliptin treated rats after 8 weeks of MS to the end of 12 weeks. Group VI (prophylactic): Curcumin is administered with MS induction concomitantly for 12 weeks. Transthoracic echocardiogram was done while rats were alive. At the end of the experiment, blood was collected and biochemical analysis (blood glucose, serum insulin, lipid profile and cardiac enzymes) was done. Heart tissues were used for oxidative stress parameters (cardiac mitochondrial reactive oxygen species (ROS) and cardiac mitochondrial complex I and complex II) beside histopathological examination.

Results: High fat diet (HFD) administration resulted in a significant increase in blood glucose, serum insulin, homeostasis model assessment of IR (HOMA- IR) index with disturbed lipid profile. Significant increase in serum cardiac enzymes and oxidative stress tissue markers were also noticed. Echocardiography revealed structural and functional cardiomyopathy. Histopathological examination showed cellular infiltrations with fat cells and collagen fibers accumulation. DPP- 4 inhibitors and curcumin resulted in a significant decrease in glucose, insulin, and HOMA- IR index, partial amelioration of lipid profile, cardiac enzymes, and cardiac oxidative stress markers. Echocardiography revealed alleviation of cardiomyopathy. Histopathological examination also revealed highly manifested structural improvement.

Conclusion: The current study revealed that both DPP- 4 inhibitors and curcumin improve cardiomyopathy resulted from HFD administration with a diversity of mechanisms including anti-inflammatory, anti-apoptotic and anti-oxidative ways.

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INTRODUCTION

Metabolic syndrome (MS) has emerged as a major health concern worldwide. The problem of MS has been the main cause of high mortality and morbidity [1]. The prevalence of MS among Egyptian adolescents was 7.4% [2].

Consumption of a diet that is high in energy, fat, protein and sugars, but low in fruits and vegetables, increases the risk of insulin resistance (IR) [3]. Insulin resistance is the main etiology related to MS and its associated

cardiomyopathy [4]. Echocardiography is the gold-standard tool to identify abnormalities associating cardiomyopathy in addition to biomarkers [5].

Dipeptidyl peptidase-4 inhibitors (e.g. vildagliptin) are widely used oral hypoglycemic agents that are favored due to their low risk of hypoglycemia and weight gain [6]. Dipeptidyl peptidase-4 inhibitors are reported to have numerous biological roles in previous studies as a neuroprotective, anti-inflammatory, and anti-atherosclerotic effects. Moreover, they improved streptozotocin induced Alzheimer's disease, improved memory and learning impairment and brain inflammation [7].

Herbals are nowadays used in wide ranges for medical purposes lacking the side effects on the prolonged administrations of synthetic drugs, so we attended to try another natural agent which is curcumin herb. Curcumin is extracted from the rhizome of Zingiberaceae plants and has many pharmacological properties, antioxidant, anti-cancer, anti-inflammatory, cyto-protective and anti-depressant [8]. Moreover, many studies assumed that curcumin may be protective against inflammation of liver and hepatic stellate cells activation [9].

MATERIAL and METHODS
Experimental design: 60 adult male albino rats weighing 120 – 150 g were obtained, housed in wire covered cages in a room with controlled humidity, maintained at constant room temperature under suitable illumination conditions (day and night). They were kept for one week on their normal diet and free access to water for acclimatization before starting the experiment. All procedures were approved by the Animal Care Committee of Al-Azhar University, as well as specific national laws where applicable. The rats were divided into six equal groups as follows:

- **Group I (Control):** Rats fed on normal rat chow.
- **Group II (MS induced group):** Rats were fed on western rat diet, had an Atwater fuel energy of 4.6 kcal/g and comprised 50% crude carbohydrate, 21.4% crude fat, 17.5% crude protein, 3.5% crude fibre, and 4.1% ash for 12 weeks [10].
- **Group III (Vildagliptin only):** Rats were fed on normal rat chow and then administrated with vildagliptin (3mg/kg/day) dissolved into 0.9% normal saline solution via oral gavage feeding once a day for 4 weeks [11]. (Manufactured by Novartis Pharma Stein AG, Stein, Switzerland)
- **Group IV (Curcumin only):** Rats received curcumin 250 mg/kg orally for 12 weeks [12].
- **Group V (Therapeutic):** Rats in this group received western rat diet, had an Atwater fuel energy of 4.6 kcal/g and comprised 50% crude carbohydrate, 21.4% crude fat, 17.5% crude protein, 3.5% crude fibre, and 4.1% ash for 12 weeks [10], after 8 weeks vildagliptin (3 mg/kg/day) was dissolved into 0.9% normal saline solution and was given via oral gavage feeding once a day for 4 weeks [11].

- **Group VI (Prophylactic):** The rats in this group received western rat diet, had an Atwater fuel energy of 4.6 kcal/g and comprised 50% crude carbohydrate, 21.4% crude fat, 17.5% crude protein, 3.5% crude fibre and 4.1% ash for 12 weeks [10] with administration of curcumin 250mg/ kg orally for 12 weeks (the same period) [12].

Drugs and Herb: Vildagliptin (3mg/kg/day) (Galvus, Novartis) was dissolved into 0.9% normal saline solution [13] and was given via oral gavage feeding once a day for 4 weeks [11]. Curcumin was purchased from spice dealer, suspended in saline, and was given via oral gavage [14] and was given for 12 weeks [15]. Curcumin dose was calculated according to the weight of rats and suspended in 0.9% normal saline (e.g. if the rat weighs 150 gm, curcumin dose for this rat will be 37.5 mg suspended in 1 ml saline given by oral gavage). Before scarification, transthoracic 2D mode echo-cardiogram was done to measure: left ventricular posterior wall thickness at end-diastole (LVPWd), left ventricular dimensions at end-systole (LVDs), left ventricular posterior wall thickness at end-systole (LVPWs), ejection fraction (EF %) and fractional shortening (FS %) [16].

At the end of the experiment, blood was collected from the tail vein. Serum was separated and stored frozen at -80ºC until the time of analysis to assess 1- the occurrence of MS through: parameters of IR (glucose, insulin and homeostasis model assessment of IR (HOMA- IR) index) and parameters of lipid profile (triglycerides (TG), total cholesterol (TC) and high density lipoprotein (HDL)) 2- cardiac functions by estimating: cardiac enzymes lactate dehydrogenase (LDH) and creatine kinase (CK- MB) levels [17]. Animal's chest was opened; the heart was isolated and was longitudinally cut. One half was used for estimation of tissue parameters: cardiac mitochondrial reactive oxygen species (ROS), cardiac mitochondrial complex I and complex II and the other half was used for histopathological examination.

Biochemical measurements:
1. **Parameters investigating IR:** The serum glucose was assayed colorimitrically by the method adopted by Tietz [18]. Insulin concentrations were measured in serum samples by enzyme immunoassay using the rat insulin ELISA kits [19] and HOMA-IR index was calculated using the equation: (Insulin in µIU/L) × (glucose in mmol/L) divided by 22.5 [20].
2. **Parameters investigating Lipid profile:** TG level was measured in plasma by quantitative- enzymatic - colorimetric procedure according to the method of França et al. [21] using a triglycerides colorimetric assay kit from Cayman Chemical Company. TC level was measured in plasma by quantitative - enzymatic - colorimetric procedure according to the method of MacLachlan et al. [22] using a cholesterol quantitation kit from Calbiochem Company and HDL-C was measured in plasma by quantitative - enzymatic

colorimetric procedure according to the method of Trinder [23] using a HDL-C kit from Bio Med diagnostic Company.

3. **Parameters investigating cardiac function:** The activity of the enzyme LDH was estimated by the method of Teitz [24] using agape Diagnostic Kit and CK-MB was measured by immune-enzymatic method [25].

4. **Tissue samples:** estimation of mitochondrial ROS is based on the sandwich ELISA principle, mitochondrial complex I and complex II using Isolation Kit for Tissue & Cultured Cells (BV cat # K288-50) or Yeast Mitochondria Isolation Kit (BV cat # K259-50).

Histopathological examination

Light microscopic examination: At the end of the experiment, animals were subjected to diethyl ether light anesthesia and then were sacrificed**.** Animal's chest was opened; the heart was isolated and was longitudinally cut. Half of the heart was used for histopathological examination: fixed in 10% neutral buffered formalin, embedded in paraffin. Sections were cut at 5μm thickness, then stained with hematoxylin and eosin (H and E) and

Sirius red staining and were examined by light microscope [26].

Statistical analysis

Data recorded as mean ± standard deviation (S.D.). Comparison was done between 2 groups by Student's t-test (P<0.05 was considered as significant).

RESULTS

I. High fat diet administration for 12 weeks resulted in manifested MS proved by a significant increase in blood glucose, serum insulin, HOMA- IR, serum TG and TC and significant decrease in serum HDL. Cardiac dysfunction was indicated by a significant elevation of serum cardiac enzymes (LDH and CK- MB) levels, elevation of tissue levels of cardiac mitochondrial ROS, and of marked decrease in levels of cardiac mitochondrial complex I and complex II. Alterations in the echo findings as significant decrease in EF% and FS% and a significant increase in LVPWd, LVDs and LVPWs that suggest occurrence of functional and structural cardiomyopathy (left ventricular hypertrophy (LVH) and systolic dysfunction) compared to control group.

Table (1): Alteration of insulin resistance and lipid profile parameters, blood glucose (mmol/ L), serum insulin (μIU/ L) HOMA- IR, serum triglycerides, serum total cholesterol and serum HDL (mg/ dl) in different groups

Groups	Control group (No.= 10)	Vildagliptin only group (No.= 10)		Curcumin only Group (No.= 10)		MS induced Group (No.= 10)		Therapeutic group (No.= 10)			Prophylactic group (No.= 10)		
Parameters	Mean ±SD	Mean ±SD	P value control group	Mean ±SD	P value control group	Mean ±SD	P value control group	Mean ±SD	P value MS induced group	P value vildagliptin only group	Mean ±SD	P value MS induced group	P value curcumin Only group
Glucose (mmol/L)	5.9±0.5	5.9± 0.4	> 0.05	5.7 ± 0.5	> 0.05	15.01 ± 2.1d	< 0.05	9.8± 1.2a, c	< 0.05	< 0.05	9.7± 1.9a, b	< 0.05	< 0.05
Insulin (μIU/mL)	8.3± 1.3	9.1± 0.9	> 0.05	8.8 ± 0.5	> 0.05	19.9± 1.6d	< 0.05	11.5± 2.01a, c	< 0.05	< 0.05	11.5± 1.5a, b	< 0.05	< 0.05
HOMA- IR	2.2± 0.4	2.4 ±0.3	> 0.05	2.3 ± 0.2	> 0.05	13.3± 2.5d	< 0.05	5.1± 1.2a, c	< 0.05	< 0.05	5.02± 1.3a, b	< 0.05	< 0.05
Serum TG (mg /dl)	74.4 ±2.7	64.05 ± 8.6d	< 0.05	71.8 ±6.1	> 0.05	129.9 ±31.9d	< 0.05	84.3± 7.1**a, c**	< 0.05	< 0.05	82.2 ± 10.4a, b	< 0.05	< 0.05
Serum TC (mg / dl)	139.7 ±7.6	137.4 ±6.7	> 0.05	139.6 ± 10.6	> 0.05	244.6 ±34.3d	< 0.05	180.6± 4.6**a, c**	< 0.05	< 0.05	182.7± 14.2a, b	< 0.05	< 0.05
Serum HDL (mg / dl)	62.5 ±3.6	64.3 ± 7.1	> 0.05	62.1 ± 6.3	> 0.05	30.9 ± 4.8d	< 0.05	47.9± 3.8a, c	< 0.05	< 0.05	52.4± 7.8a, b	< 0.05	< 0.05

Data were analyzed through student's T-test between 2 groups. P. value < 0.05 was significant, a: significant values versus MS group, b: significant values versus curcumin only group, c: significant values versus vildagliptin only group, d: significant values versus control group.

II. Vildagliptin administration for 4 weeks, after the occurrence of MS, resulted in improvement of MS (manifested by significant decrease of blood glucose, serum insulin, HOMA- IR, TG and TC) and a significant increase in serum HDL. Improvement of cardiac dysfunction was shown by significant lowering of serum cardiac enzymes LDH and CK- MB levels, and cardiac mitochondrial ROS, accompanied with significant

increase in levels of cardiac mitochondrial complex I and complex II. Echo findings showed a significant increase in EF% and FS% and a significant decrease in LVPWd, LVDs and LVPW when compared to MS induced group.

III. Curcumin administration for 12 weeks resulted in improvement of MS manifested by significant decrease of blood glucose, serum insulin, HOMA- IR, Serum TG

and TC, and significant increase in HDL. Improvement of cardiac dysfunction proved by significant lowering of serum cardiac enzymes LDH and CK- MB levels, and cardiac mitochondrial ROS, with significant increase levels of cardiac mitochondrial complex I and complex II. Echo findings showed a significant increase in EF%

and FS% and a significant decrease in LVPWd, LVDs and LVPW when compared to MS induced group.

IV. Comparing DPP- 4 inhibitors administration and curcumin administration showed non-significant changes in all measured parameters, except that curcumin succeeded to return EF% and FS% to control levels.

Table (2): Alteration of parameters evaluating cardiac functions, serum LDH, CK- MB, mitochondrial ROS, mitochondrial complex I and complex II (mg/ dl) in different groups

Groups	Control group (No.=10)	Vildagliptin only group (No.= 10)		Curcumin only group (No.= 10)		MS induced group (No.= 10)		Therapeutic group (No.= 10)			Prophylactic group (No.= 10)		
Parameters	Mean ±SD	Mean ±SD	P value control group	Mean ± SD	P value control group	Mean ±SD	P value control group	Mean ±SD	P value MS induced group	P value vildag-liptin only group	Mean ±SD	P value MS induced group	P value curcumin only group
Serum LDH (mg/ dl)	119.7 ± 5.6	118.1 ± 7.9	> 0.05	118.4 ± 5.2	> 0.05	280.9 ± 48.3[d]	< 0.05	194.3± 10.4[a,c]	< 0.05	< 0.05	193.6± 12.4[a, b]	< 0.05	< 0.05
Serum CK- MB (mg/ dl)	113.7 ± 2.8	109.3 ± 3.4[d]	< 0.05	113.3 ± 6.6	> 0.05	232.4 ± 16.5[d]	< 0.05	157.9± 10.3[a, c]	< 0.05	< 0.05	152.5± 12.4[a, b]	< 0.05	< 0.05
Mitochondrial ROS (mg/ dl)	43.5 ± 8.01	33.2 ± 2.9[d]	< 0.05	35.4 ± 3.7[d]	< 0.05	111.2 ± 18.2[d]	< 0.05	70.09± 14.9[a,c]	< 0.05	< 0.05	65.4± 13.9[a, b]	< 0.05	< 0.05
Mitochondrial complex I (mg/ dl)	35.6 ± 9.6	43.3 ± 12.6	> 0.05	51.5 ± 8.8[d]	< 0.05	18.8 ± 2.08[d]	< 0.05	36.4± 8.2[a]	< 0.05	> 0.05	41.4± 4.7[a,b]	< 0.05	< 0.05
Mitochondrial complex II (mg/d)	72.5 ±11.1	81.8 ± 7.9[d]	< 0.05	79.6 ± 9.6	> 0.05	37.4 ± 5.03[d]	< 0.05	63.3± 8.3[a,c]	< 0.05	< 0.05	64.6± 9.7[a,b]	< 0.05	< 0.05

Data were analyzed through student's T-test between 2 groups. P. value < 0.05 was significant, a: significant values versus MS group, b: significant values versus curcumin only group, c: significant values versus vildagliptin only group, d: significant values versus control group

Table (3): Alteration of all the measured echocardiographic parameters in different groups

Groups	Control group No.= 10	Vildagliptin only group (No.= 10)		Curcumin only group (No.= 10)		MS induced group (No.= 10)		Therapeutic group (No.= 10)			Prophylactic group (No.= 10)		
Parameters	Mean ±SD	Mean± SD	P value control group	Mean ±SD	P value control group	Mean ±SD	P value control group	Mean ±SD	P value MS induced group	P value vildag-liptin only group	Mean ±SD	P value MS induced group	P Value curcumin only group
EF %	81.3 ± 3.7	81.1 ± 1.8	> 0.05	79.6 ± 0.7	> 0.05	67.9 ± 3.3[d]	< 0.05	78.33± 0.95 [a,c]	< 0.05	< 0.05	80.25 ±1.36[a]	< 0.05	> 0.05
FS %	45.6± 4.5	45.5 ± 1.9	> 0.05	43.2 ± 0.8	> 0.05	32.1 ± 2.2[d]	< 0.05	39.9 ±1.6 [a,c]	< 0.05	< 0.05	42.5± 1.34[a]	< 0.05	> 0.05
LVPWd (cm)	0.25± 0.06	0.29 ±0.1	> 0.05	0.26 ±0.1	> 0.05	0.29 ± 0.03[d]	< 0.05	0.26± 0.05[a]	< 0.05	> 0.05	0.26± 0.05[a]	< 0.05	> 0.05
LVDs (cm)	0.14± 0.05	0.13 ± 0.0	> 0.05	0.14 ± 0.0	> 0.05	0.18 ± 0.02[d]	< 0.05	0.14± 0.01[a]	< 0.05	> 0.05	0.13± 0.02[a]	< 0.05	= 0.05
LVPWs (cm)	0.28± 0.06	0.28 ± 0.0	> 0.05	0.26 ± 0.1	> 0.05	0.32 ± 0.04[d]	< 0.05	0.28± 0.04 [a,c]	< 0.05	< 0.05	0.28± 0.05[a]	< 0.05	> 0.05

Data were analyzed through student's T-test between 2 groups. P. value < 0.05 was significant, a: significant values versus MS group, c: significant values versus vildagliptin only group, d: significant values versus control group

V. Histopathological examination is illustrated in the following figures
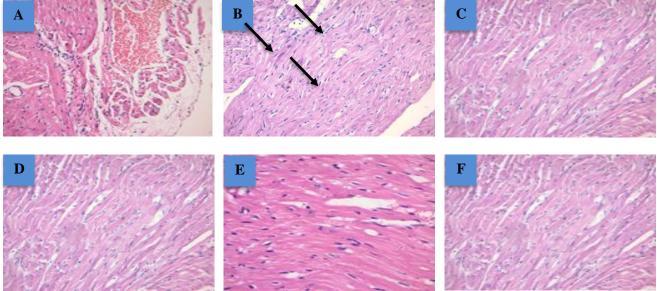

Figure (1): Microscopic examination of cardiac tissues: (A) Control group showing long and cylindrical muscle fibers with central nuclei, (B) MS induced group showing cellular infiltration, congested blood vessel and widely separated pericardium (arrows). (C)Vildagliptin only group showing long, cylindrical muscle fibers with central nucleus and single endothelial cells lining blood vessels, (D) Curcumin only group showing long, cylindrical muscle fibers with central nuclei and single endothelial cells lining the blood vessel group, (E) Therapeutic group showing long, cylindrical muscle fibers with central nucleus and congested blood vessels lined with single endothelial cells, and (F) Prophylactic group showing long, cylindrical muscle fibers with central nucleus, congested blood vessels and fat cells (H and E, X 100).
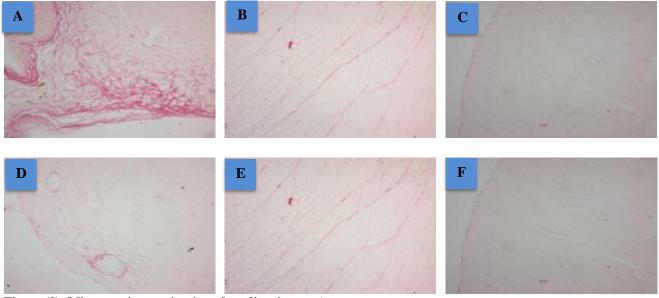

Figure (2): Microscopic examination of cardiac tissues: (A) Control group showing few collagen fibers appear red and the rest of structures appear yellow, (B) MS induced group showing amorphous collagen fibers appears red, (C)Vildagliptin only group showing few collagen fibers appears red, (D) Curcumin only group showing few collagen fibers appears red around the muscle fibers and pericardium, (E) Therapeutic group showing few collagen fibers appear red around blood vessels, and (F) Prophylactic group showing few collagen fibers appear red around blood vessels mainly (Sirius red, X 200).

DISCUSSION

Previous studies assumed that impaired insulin effect on the adipocyte could disturb fatty acids metabolism thus it will be directed towards re-esterification causing intracellular steatosis and accumulation of complex lipids in other tissues that might exacerbate IR. [27].

Histopathological examination of the present study could support this view as it revealed fat accumulation in cardiac tissue of MS induced group. The presence of high insulin levels in MS rats could predispose to further IR as the studies explained that impaired insulin signaling in

the brain leads to failure to suppress appetite and consequently adjust nutrient sensing that contributes to obesity[28]. This impairment could also eliminate the ability of insulin to suppress hepatic glucose output.

The observed IR in the current study could be also explained by another mechanism which is the occurrence of oxidative stress and augmentation of inflammatory cytokine production with adipocyte overload. Previous study [29] related the obesity-associated development of MS to the dysregulated production of adipocytokines and the selective increase in ROS production which increased oxidative stress in accumulated fat and the net result is impairment of both insulin secretion from the pancreatic β cells and glucose transport in the cardiac muscle. This increased ROS levels may also damage proteins and induce inflammation by augmenting cytokine production from activated inflammatory cells which results in further tissue damage [30]. Studies suggested that HFD consumption increases the exposure to oxidative stress that increases a group of interleukins (IL- 1, IL-6) and tumor necrosis factor- α (TNF- α) production by increasing nuclear factor kappa- light- chain- enhancer of activated B cells (NF- kB) [31].

In the current study, there were marked alteration of the cardiac functions represented with significant elevation of serum cardiac enzymes levels (LDH and CK- MB), elevation of tissue levels of cardiac mitochondrial ROS, marked decrease in the levels of cardiac mitochondrial complex I and complex II. These alterations of the current study results correlate with the echo findings of the same present study, which revealed functional alterations represented by a significant decrease in EF% and FS% and structural alterations manifested by a significant increase in LVPWd, LVDs and LVPWs that suggest occurrence of functional and structural cardiomyopathy (LVH and systolic dysfunction).

The main pathophysiological mechanism that contributes to the development of cardiomyopathy, cardiac hyper-trophy and insulin- resistant heart is the cardiac dysmetabolism, as reported in the previous study [32]. This metabolic inflexibility caused by internalization of glucose transporter 4 (GLUT4) to its intracellular location and CD36 (mediated uptake of FAs) becomes specially localized to the sarcolemma leaving the fatty acid as the sole fuel source [33]. This shift induces an intramyocardial lipid accumulation due to the increased uptake and accumulation of lipid in the heart [34] which is correlated exactly with histopathological findings in the current study that revealed myocytes hypertrophy and many fat droplets appearance. This high lipid contents can induce contractile dysfunction independently of IR [35]. These functional changes were also correlated with the echo findings of the present study that reveals functional alterations in the form of a significant decrease in EF% and FS%.

The observed decrease in the activity of complex I and complex II, in the present study, is the main causes of mitochondrial dysfunction in the heart. Studies cleared that mitochondrial dysfunction is caused either by mutations of the genes required to generate a fully functional complexes or by a cumulative damage to the complexes [36]. Studies explained that decreased mito-chondrial complex I activity together with an increased mitochondrial protein lysine acetylation may contribute to the IR and increased FA oxidation in the cardiomyocytes [37].

All the recorded biochemical results and cardiac imaging results go in hand with observed histopathological changes of the cardiac tissue in the current study. H and E staining revealed many fat cells appeared as empty cells with peripherally flattened nuclei, highly congested blood vessels with cellular infiltrations and widely separated pericardium. These findings go in hand with previous studies [26, 38, 39]. While Sirius red staining in the current study revealed accumulation of collagen fibers, which goes in hand with previous studies [40, 41], which revealed similar findings.

Vildagliptin for 4 weeks (after MS induction) resulted in improvement of MS manifestations proved by significant decrease in IR parameters and restoration of lipid profile parameters. This manifested improvement in the tested parameters mostly refers to vildagliptin ability to improve the state of IR associates MS and may enhance insulin activity. This ability could directly balance the disturbed carbohydrate and lipid metabolism and alleviates the ectopic lipid accumulation that complicates IR. This opinion is supported by studies which assumed that vildagliptin could improve IR through its effect on incretin peptides [42]. Vildagliptin acts by increasing incretins (Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1(GLP-1)), which inhibit glucagon release and thus increase insulin secretion and decrease blood glucose levels. This better-ment of the tested IR parameters and lipid profile was accompanied by recovery of the cardiac functions, as proved by significant lowering of serum cardiac enzymes LDH and CK- MB levels when compared to MS induced group. Moreover, improvement of oxidative stress parameters was recorded after vildagliptin administration in the form of decreased tissue levels of cardiac mitochondrial ROS, with significant increase levels of cardiac mitochondrial complex I and complex II when compared to MS induced group.

These recorded improvements correlate with the present study echo findings that showed a manifested improvement of the functional changes of the heart appear as a significant increase in EF% and FS% and improve-ment of the structural changes represented by a significant decrease in LVPWd, LVDs and LVPWs when compared to MS induced group. The recorded echo changes

revealed improvement of the functional and structural cardiomyopathy manifestations (LVH and systolic dysfunction).

Vildagliptin can improve the mitochondrial biogenesis through its inhibitory action on DPP-4 enzyme [43]. This activation of GLP-1 receptors was also reported to activate the cyclic adenosine monophosphate-dependent protein kinase A (cAMP-dependent protein kinase A) which inhibits mitochondrial ROS accumulation and restore metabolic alterations [44]. Another possibility is that increased GLP-1 levels by vildagliptin could directly influence mitochondrial preservation via modifying oxidative-phosphorylation process and thus attenuating oxidative stress [45].

The observed improvement in oxidative stress parameters of the current study presented by decreased tissue levels of cardiac mitochondrial ROS, with significant increase levels of cardiac mitochondrial complex I and complex II. Studies explained that vildagliptin therapy led to a marked reduction in mitochondrial ROS production back to the normal levels, alleviated mitochondrial swelling and increased mitochondrial respiration function. Besides, vildagliptin prevents separation of NF-κB from its complex, prevents its translocation to the nucleus with the end result suppression of inflammatory cytokines [46, 47]. Another mechanism by which vildagliptin treatment was accompanied by improvement of mitochondrial functions is that vildagliptin could restore the autophagosome clearance to appropriate levels which maintain cellular homeostasis and cell survival [48]. The observed recovery of left ventricular function in the current study with vildagliptin administration could be due to attenuation of cardiac mitochondrial dysfunction as proved by the current study oxidative stress parameters (mitochondrial ROS, complex I and II).

All these biochemical improvements were associated with improvement of histopathological findings with H and E staining including decreased appearance of fat cells, decreased cellular infiltrations and congestion of blood vessels and with Sirius red staining which revealed less appearance of collagen fibers when compared to MS induced group. The current histopathological results were compatible with previous studies [49- 51].

Curcumin administration resulted in improvement of MS manifestations due to its ability to improve the state of IR associates MS that may help returning of insulin activity to some extent. This improvement of IR was supported by the previous study which revealed that curcumin could stimulate insulin release from pancreatic beta cells. In addition, curcumin may increase the peripheral insulin sensitivity, and this may explain its antidiabetic activity [52]. This mentioned ability of curcumin to modulate fat metabolism is consistence with the histopathological examination of the present study that revealed reduced appearance of fat cells in the cardiac muscle cells.

Previous studies tried to explain the ability of curcumin to ameliorate lipid profile. They assumed that curcumin could modulate the expression of genes and the activity of enzymes involved in lipoprotein metabolism that lead to a reduction in plasma TG and TC and elevate HDL-C concentrations [53, 54].

These recorded data of the present study was accompanied by significant lowering of the level of serum cardiac enzymes LDH and CK- MB which was associated with decreased tissue levels of cardiac mitochondrial ROS, and significant increase levels of cardiac mitochondrial complex I and complex II, when compared to MS induced group. These betterments in the current study recordings correlate with its echo findings that showed improvement of the functional parameters of the heart manifested by a significant increase in EF% and FS% as well as improvement of the structural changes, represented as a significant decrease in LVPWd, LVDs and LVPW, when compared to MS induced group. These recorded echo changes show improvement of functional and structural cardiomyopathy manifestations (LVH and systolic dysfunction).

Curcumin could prevent the onset of inflammation through inhibition of (NF-κB), one of the major modulators of inflammatory process, preventing its translocation to the nucleus and inhibition of the gene's expression of inflammatory cytokines [55]. The anti-inflammatory effect of curcumin was explained through its modulation on toll-like receptor 2 (TLR2), one of the major mediators of the innate immune system. Studies assumed that curcumin reduced expressions of TLR2 and decreased macrophage infiltration and the fibrotic response in cardiac tissues; hence restore heart contractility [56]. The previous mentioned anti-inflammatory activity of curcumin could be correlated exactly with the histopathological examination of the current study that revealed reduced cellular infiltrations and less appearance of collagen fibers in the cardiac cells. The recorded effects of curcumin in the current study on tissue levels of cardiac mitochondrial ROS, cardiac mitochondrial complex I and complex II could be explained by its ability to attenuate the oxidative stress. Curcumin can intercept and neutralize ROS, nitric oxide and peroxynitrite and decrease expression of NADPH oxidase, thus restore SOD activity and reduce lipid peroxidation in IR as explained by previous studies [57].
Another mechanism for the antioxidative effect of curcumin includes activation of heme oxygenase-1 and maintenance of glutathione metabolism or sweeping of ROS. Heme oxygenase-1 and glutathione are major antioxidants that prevent deteriorations of the process of MS through the mediation of the main redox regulatory signaling pathway in the cell [58]. Moreover, curcumin could scavenge a variety of ROS and reduce mitochondrial deficiency by activation of silent

information regulator 1 (SIRT1) signaling, up regulation of Bcl-2 and down regulation of Bax [55].

All these previous biochemical results in the present study are associated with improvement of the histopathological findings with H and E which revealed reduced cellular infiltrations and congestion of blood vessels and less appearance of fat cells. Sirius Red staining revealed less appearance of collagen fibers when compared to MS induced group. These findings go in hand with the previous findings [59-61].

CONCLUSION

The current study revealed that both vildagliptin and curcumin improve cardiomyopathy resulted from HFD administration with a diversity of mechanisms including anti-inflammatory and anti-apoptotic and anti-oxidative ways. Curcumin succeeded to restore function and structure of the heart, while vildagliptin fails to return functional abnormalities to the control levels. As prevention is better than cure, curcumin as an herb with less side effects is recommended as a protective agent for people susceptible to MS with cardiac complications compared to vildagliptin.

Future directions

- Further studies are needed to clarify more values of curcumin to answer many of open issues about its biological effects.

REFRENCES

1. **Saklayen MG.** The global epidemic of the metabolic syndrome. Curr Hyperten Rep 2018; 20 (2):12.
2. **Ali F, Ismail M, Abd EL-Azeem E, Abdulla A, Seoudi D, Abd EL- Rahman S.** Obesity and metabolic syndrome among Egyptian adolescents. International Journal of Scientific and Engineering Research 2014; 5(2):1512-1523.
3. **Badoud F, Lam KP, Perreault M, Zulyniak MA, Britz-McKibbin P, Mutch DM.** Metabolomics reveals metabolically healthy and unhealthy obese individuals differ in their response to a caloric challenge. PLoSOne 2015; 10, e0134613.
4. **Hwang HR, Jeong DW, Kim YJ, Lee S, Lee JG, Kang Y et al.** Comparison of insulin resistance and metabolic syndrome criteria in metabolically obese, normal weight (MONW) individuals in the prediction of cardiovascular disease risk: analysis of the Korean National Health and Nutrition Examination Survey (KNHANES) in 2010–2012. Int J Diabetes Dev Ctries 2018; 38(1):88–94.
5. **Guanghong J, Michael A, James R.** Diabetic cardiomyopathy. Circ Res. 2018; 122 (4):624-638.
6. **Phung O, Scholle J, Talwar M, Coleman C.** Effect of noninsulin antidiabetic drugs added to metformin therapy on glycemic control, weight gain, and hypoglycemia in type 2 diabetes. JAMA 2010; 303: 1410–1418.
7. **Jain S and Sharma B.** Neuroprotective effect of selective DPP-4 inhibitor in experimental vascular dementia. Physiol. Behav. 2015; 152: 182–193.
8. **Panahi Y, Hosseini M, Khalili N, Naimi E, Majeed M, Sahebkar A.** Antioxidant and anti-inflammatory effects of curcuminoid-piperine combination in subjects with metabolic syndrome: A randomized controlled trial and an updated meta-analysis. Clinical Nutrition 2015; 34 (6): 1101–1108.
9. **García-Niño W, Tapia E, Zazueta C, Zatarain-Barrón Z, Hernández-Pando R, Vega-García C.** Curcumin pretreatment prevents potassium dichromate-induced hepatotoxicity, oxidative stress, decreased respiratory complex I activity, and membrane permeability transition pore opening. Evid Based Complement Alternat Med 2013; 424692**.
10. **Auberval N, Dal S, Maillard E, Bietiger W, Peronet C, Pinget M et al.** Beneficial effects of a red wine polyphenol extract on high-fat diet-induced metabolic syndrome in rats. Eur J Nutr 2017; 56:1467–1475.
11. **Tanajak P, Pintana H, Siri-Angkul N, Khamseekaew J, Apaijai N, Chattipakorn S et al.** Vildagliptin and caloric restriction for cardioprotection in pre-diabetic rats. Journal of Endocrinology 2017; 232: 189–204.
12. **Su L, Wang Y, Chi H.** Effect of curcumin on glucose and lipid metabolism, FFAs and TNF-α in serum of type 2 diabetes mellitus rat models. Saudi Journal of Biological Sciences 2017; 24, (8): 1776-1780.
13. **Apaijai N, Pintana H, Chattipakorn S, Chattipakorn N.** Effects of vildagliptin versus sitagliptin, on cardiac function, heart rate variability and mitochondrial function in obese insulin-resistant rats. British Journal of Pharmacology 2013; 169: 1048–1057.
14. **Pan Y, Zhao D, Yu N, An T, Miao J, Mo F et al.** Curcumin improves glycolipid metabolism through regulating peroxisome proliferator activated receptor γ signaling pathway in high- fat diet- induced obese mice and 3T3- L1 adipocytes. Royal society open science publishing. R. Soc. Opensc 2017; 4:170917.

15. **Santos-Parker JR, Strahler TR, Bassett CJ, Bispham N Z, Choncho MB, Seals DR.** Curcumin supplementation improves vascular endothelial funct ion in healthy middle- aged and older adults by increasing nitric oxide bioavailability and reducing oxidative stress. AGING 2017; 9(1):187.

16. **Chang W, Xiao D, Ao X, Li M, Xu T, Wang J.** Increased dynamin-related protein 1–dependent mitochondrial fission contributes to high-fat-diet-induced cardiac dysfunction and insulin resistance by elevating tafazzin in mouse hearts. Mol. Nutr. Food Res 2019; 63:1801322.

17. **[Tunapong W, Apaijai N, Yasom S, Tanajak P, Wanchai K, Chunchai T et al.** Chronic treatment with prebiotics, probiotics and synbiotics attenuated cardiac dysfunction by improving cardiac mitochondrial dysfunction in male obese insulin-resistant rats. Eur J Nutr 2017; 57(6):2091-2104.

18. **Tietz NW.** Clinical Guide to Laboratory tests. 3rd ed. Philadelphia. WB. Saunders 1995; 268-273 pp.

19. **Carlsson A, Hallgren IB Johansson H, Sandler S.** Concomitant enzyme-linked immunosorbent assay measurements of rat insulin, rat c-peptide, and rat proinsulin from rat pancreatic islets: effects of prolonged exposure to different glucose concentrations. Endocrinology 2010; 151(10):5048-5052.

20. **Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC.** Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985; 28 (7):412-9.

21. **França CN, Mendes CC, Ferreira CE.** Time collection and storage conditions of lipid profile. Braz. J. Med. Biol. Res 2018; 51(3): e6955.

22. **MacLachlan J, Wotherspoon AT, Ansell RO, Brooks CJ.** Cholesterol oxidase: sources, physical properties, and analytical applications. J Steroid Biochem Mol Biol 2000; 72(5):169-195.

23. **Trinder P.** Determination of glucose in blood using glucose oxidase with on alternative oxygen receptor. Ann. Clin. Biochem1969; 6: 24-27.

24. **Teitz NW.** In Fundamentals of clinical chemistry, WB Saunders and company, Philadelphia 1976; 602-603.

25. **Okinaka S, Kumagai H, Ebashi S, Sugita H, Momoi H, Toyokura Y et al.** Serum creatine phosphokinase activity in progressive muscular dystrophy and neuromascular diseases. Arch Neurol 1961; 4:250-255**.**

26. **Abbas AM, Sakr HF.** Simvastatin and vitamin E effects on cardiac and hepatic oxidative stress in rats fed on high fat diet. J Physiol Biochem 2013; 69:737–750.

27. **El-Assaad W, Joly E, Barbeaum A.** Glucolipo-toxicity alters lipid partitioning and causes mitochondrial dysfunction, cholesterol, and ceramide deposition and reactive oxygen species production in INS832/13 beta-cells. Endocrinology 2010; 151: 3061-3073.

28. **Rask-Madsen C, Kahn C.** Tissue-specific insulin signaling, metabolic syndrome and cardiovascular disease. Arterioscler Thromb Vasc Biol 2012; 32(9): 2052–2059.

29. **Furukawa S, Matsuda M, Shimomura I.** Increased oxidative stress in obesity and its impact on metabolic syndrome. J Clin Invest 2107; 114 (12):1752-1761.

30. **Tse E, Tran D, Kim M, Belsham D.** Diet-induced cellular neuroinflammation in the hypothalamus: Mechanistic insights from investigation of neurons and microglia. Molecular and Cellular Endocrinology 2016; 438: 18-26.

31. **Cortez M, Carmo L, Rogero M, Borelli P, Fock R.** A high-fat diet increases IL- 1, IL- 6 and TNF- alpha production by increasing NF- kappaB and attenuating PPAR-gamma expression in bone marrow mesenchymal stem cells. Inflammation 2013; 36:379-386.

32. **Delbridge LM, Benson VL, Ritchie RH, Mellor KM.** Diabetic cardiomyopathy: the case for a role of fructose in disease etiology. Diabetes 2016; 65:3521–3528.

33. **Battiprolu P, Lopez-Crisosto C, Wang Z, Nemchenko A, Lavandero S and Hill J.** Diabetic cardiomyopathy and metabolic remodeling of the heart. Life Sci 2013; 92:609-615.

34. **D'Souza K, Nzirorera C and Kienesberger P.** Lipid metabolism and signaling in cardiac lipotoxicity. Biochem Biophys Acta 2016; 1860 (10): 1513–24.

35. **Liu Y, Neumann D, Glatz J and Luiken J.** Molecular mechanism of lipid induced cardiac insulin resistance and contractile dysfunction. Prostaglandins Leukot Essent Fatty Acids 2016; 136: 131-141.

36. **Chouchani E, Methner C, Buonincontri G, Hu C, Logan A, Sawiak S et al.** Complex I deficiency due to selective loss of Ndufs 4 in the mouse heart results in severe hypertrophic cardiomyopathy. PLoSOne 2014; 9: e94157.

37. **Vazquez E, Berthiaume J, Kamath V, Achike O, Buchanan E, Montano M et al.** Mitochondrial complex I defect and increased fatty acid oxidation enhances protein lysine acetylation in the diabetic heart. Cardiovasc Res 2015; 107:453–465.

38. **Bhandari U, Chaudhari H, Bisnoi A, Kumar V, Khanna G, Javed K.** Anti-obesity effect of standardized ethanol extract of Embelia ribes in murine model of high fat diet-induced obesity. Pharma Nutrition 2013; 1 (2): 50-57.

39. **Udomkasemsab A, Ngamlerst C, Adisakwattana P, Aroonnual A, Tungtrongchitr R, Prangthip P.** Maoberry (Antidesma bunius) ameliorates oxidative stress and inflammation in cardiac tissues of rats fed a high-fat diet. Udomkasemsab et al. BMC Complementary and Alternative Medicine 2018; 18: 344.

40. **Wu F, Wang B, Zhang S, Shi L, Wang Y, Xiong R et al.** FGF21 ameliorates diabetic cardiomyopathy by activating the AMPK-paraoxonase 1 signaling axis in mice. Clinical Science 2017; 131: 1877-1893.

41. **Marín-Royo G, Ortega-Hernández A, Martínez-Martínez E, Jurado-López R, Luaces M, Islas F et al.** The impact of cardiac lipotoxicity on cardiac function and mirnas signature in obese and non-obese rats with myocardial infarction. Scientific Reports J 2018; 9(1):444.

42. **Lovshin J, Zinman B.** Blood pressure-lowering effects of incretin- based diabetes therapies, Can. J. Diabetes 2014; 38: 364–371.

43. **Takada S, Masaki Y, Kinugawa S, Matsumoto J, Furihata T, Mizushima W et al.** Dipeptidyl peptidase-4 inhibitor improved exercise capacity and mitochondrial biogenesis in mice with heart failure via activation of glucagon-like peptide-1 receptor signaling. Cardiovasc Res 2016; 111: 338–347.

44. **[Saeid F, Aniseh J, Reza B, Manouchehr V.** Signaling mediators modulated by cardioprotective interventions in healthy and diabetic myocardium with ischaemia-reperfusion injury. Eur J Prev Cardiol 2018; 25(14):1463–1481.

45. **Home P.** Cardiovascular outcome trials of glucose-lowering medications: an update. Diabetologia 2019; 62(3):357–369.

46. **Kimura S, Inoguchi T, Yamasaki T, Yamato M, Ide M, Sonoda N.** A novel DPP-4 inhibitor teneligliptin scavenges hydroxyl radicals: In vitro study evaluated by electron spin resonance spectroscopy and in vivo study using DPP-4 deficient rats. Metabolism 2016; 65(3): 138–145.

47. **Zhang X, Zhang Z, Zhao Y, Jiang N, Qiu, J, Yang Y et al.** Alogliptin, a dipeptidyl peptidase-4 inhibitor, alleviates atrial remodeling and improves mitochondrial function and biogenesis in diabetic rabbits. Journal of the American Heart Association 2017; 1: 17; 6:e005945.

48. **Xie J, Cui K, Hao H, Zhang Y, Lin H, Chen Z.** Acute hyperglycemia suppresses left ventricular diastolic function and inhibits autophagic flux in mice under prohypertrophic stimulation. Cardiovasc Diabetol 2016; 15(1):136.

49. **Hirakawa H, Zempo H, Ogawa M, Watanabe R, Suzuki JI, Akazawa H.** A DPP-4 Inhibitor suppresses fibrosis and inflammation on experimental autoimmune myocarditis in mice. PLoSONE 2015; 10(3): e0119360.

50. **Moon JY, Woo JS, Seo JW, Lee A, Kim DJ, Kim YG.** The dose-dependent organ specific effects of a dipeptidyl peptidase-4 inhibitor on cardiovascular complications in a model of type 2 diabetes. PLoSONE 2016; 11(3): e0150745.

51. **Borde MK, Mohanty IR, Maheshwari U, Suman RK, Deshmukh YA.** Natural dipeptidyl peptidase-4 inhibitor Terminalia arjuna mitigates myocardial infarction co-existing with diabetes in experimental rats. J Diabetes Metab Disord Control 2018; 5 (2):48–56.

52. **Shao W, Yu Z, Chiang Y, Yang Y, Chai T, Foltz W et al.** Curcumin prevents high fat diet induced insulin resistance and obesity via attenuating lipogenesis in liver and inflammatory pathway in adipocytes. PLoSOne 2012; **7**: e28784.

53. **Mohammadi A, Sahebkar A, Iranshahi M, Amini M, Khojasteh R, Ghayour-Mobarhan M et al.** Effects of supplementation with curcuminoids on dyslipidemia in obese patients: A randomized crossover trial. Phytother. Res 2013; 27: 374–379.

54. **Sahebkar A.** Curcuminoids for the management of hypertriglyceridaemia. Nat Rev Cardiol 2014; 11: 123.

55. **Mokhtari-Zaer A, Marefati N, Atkin S, Butler A, Sahebka A.** The protective role of curcumin in myocardial ischemia–reperfusion injury. J Cell Physiol 2018; 234: 214–222.

56. **Kim YS, Kwon JS, Cho YK, Jeong MH, Cho JG, Park JC.** Curcumin reduces the cardiac ischemia-reperfusion injury: Involvement of the toll-like receptor 2 in cardiomyocytes. The Journal of Nutritional Biochemistry 2012; 23(11): 1514–1523.

57. **Yu W, Wu J, Cai F, Xiang J, Zha W, Fan D et al.** Curcumin Alleviates Diabetic Cardiomyopathy in Experimental Diabetic Rats. PLOS ONE 2012; 7, (12): e52013.

58. **Sood P, Nahar U and Nehru B.** Curcumin attenuates aluminuminduced oxidative stress and mitochondrial dysfunction in rat brain. Neurotox Res 2011; 20(4):351–361.

59. **Benzer F, Kandemir F, Ozkaraca M, Kucukler S, Caglayan C.** Curcumin ameliorates doxorubicin-induced cardiotoxicity by abrogation of inflammation, apoptosis, oxidative DNA damage, and protein oxidation in rats. J Biochem Mol Toxicol. 2018; 32: e22030.

60. **Ciftci O, Turkmen N, Taslıdere A.** Curcumin protects heart tissue against irinotecan-induced damage in terms of cytokine level alterations, oxidative stress, and histological damage in rats. Naunyn-Schmiedeberg's Archives of Pharmacology 2018; 391:783–791.

61. **Apaydin F, Aslanturk A, Uzunhisarcikli M, Bas H, Kalender S, Kalender Y.** Histopathological and biochemical studies on the effect of curcumin and taurine against bisphenol A toxicity in male rats. Environmental Science and Pollution Research, 2019;26 (12): 12302-12310

الملخص العربي

تأثير مثبطات الدايبيبتديل ببتيداز٤ أو الكركمين علي متلازمة الأيض الناتجة من الغذاء والمصحوبه باختلال وظائف القلب في الفئران

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ملخص البحث

الخلفية: تعد متلازمة الأيض من العوامل المتسببة في حدوث الأمراض القلبية والتي بدورها تعد من الأسباب الرئيسيه للوفاة علي مستوي العالم.

الهدف: تهدف الدراسة الحالية هوفحص التأثير العلاجي لمثبطات الدايبيبتديل ببتيداز- ٤ والتأثير الوقائي للكركمين على النظام الغذائي الذي يسبب مرض متلازمة الأيض المرتبط باختلال وظائف القلب.

الطرق: تم تقسيم ستين من ذكور الجرذان البالغة إلى 6 مجموعات عشرة فئران لكل مجموعه: المجموعة الأولى (مجموعة ضابطة)، المجموعة الثانية (المجموعة المستحثة بمرض متلازمة الأيض)، المجموعة الثالثة (فيلداجليبتين فقط)، المجموعة الرابعة (الكركمين فقط)، المجموعة الخامسة (العلاجية) تلقت العلاج بعد ثمان أسابيع من متلازمة الأيض لنهاية الاسبوع الثاني عشر، المجموعة السادسة (الوقائية) تلقت الكركمين بالتزامن مع حث متلازمة الأيض لمدة 12 اسبوع.

تم إجراء مخطط صدى القلب بوضع ثنائي الأبعاد عبر الصدر. في نهاية التجربة ،تم تجميع عينات الدم واستخدامه لتقييم مستوي الجلوكوز والانسولين ودلالات مستوي الدهون وانزيمات القلب. واستخدمت القلوب لقياس دلالات الأنسجة لتقييم حالة الإجهاد التأكسدي القلبي، ومركبات الميتوكوندريا القلبي الاول والثاني. الي جانب الفحص التشريحي للانسجة.

النتائج: تناول الغذاء عالي الدهون نتج عنه ارتفاع كبير في نسبة السكر والأنسولين في الدم و معادلة مقاومة الانسولين وكان هناك اضطراب في مستوى الدهون، كما لوحظ ارتفاع كبير في مستويات إنزيمات القلب وارتفاع عوامل الاكسده في الأنسجة. وكذلك كشفت نتائج تخطيط صدى القلب وجود خلل هيكلي ووظيفي بعضلة القلب. أما الفحص التشريحي فأظهرالعديد من الخلايا الدهنية ، وأوعية دموية شديدة الازدحام بالخلايا وتراكم للكولاجين. وأظهر تناول مثبطات الدايبيبتدايل ببتيداز-٤والكركمين انخفاضا ملحوظا في مستويات السكر والأنسولين في الدم و معادلة مقاومة الانسولين وتحسنا طفيفا في مستوى الدهون، ومستويات إنزيمات القلب وعوامل الاكسده. وكذلك كشفت نتائج تخطيط صدى القلب التخفيف من اعتلال عضلة القلب. وأظهر الفحص التشريحي تحسنا ببناء عضلة القلب.

الاستنتاجات:أظهرت الدراسة الحالية أن تناول مثبطات الدايبيبتيدايل ببتيداز- ٤وكذلك الكركمين يحسن من اعتلال عضلة القلب من خلال مجموعة من الآليات متضمنة مضادات الالتهاب ومضادات موت الأنسجه ومضادات الأكسده.

الكلمات المفتاحية: اعتلال عضلة القلب، الكركمين، غذاءعالي الدهون، متلازمة الأيض، فيلداجلبتين.

الباحث الرئيسي

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