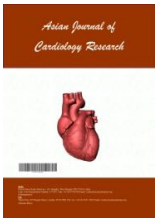

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A 4-Week Period of Administration of Fenugreek Oil or Metformin Improve Cardiac and Renal Complications in Metabolic Syndrome-Induced Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Author EAZ designed the study, performed the statistical analysis, wrote the protocol, managed the analyses of the study, managed the literature searches and wrote the first draft of the manuscript. Authors HAAEIL and AAAS designed the study, wrote the protocol and reviewed the first draft of the manuscript and author AEMKEl-M managed the analyses of the study. Author AAZ managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Frequent consumption of fructose and saturated fatty acids increase risk of metabolic syndrome (MS). Features of MS include insulin resistance, dyslipidemia, visceral obesity, and hypertension.
Aim: The aim of this study was to investigate the role of fenugreek oil and metformin in ameliorating features of MS.

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Methods: Induction of MS in rats by high-fructose high-fat fed diet was certain after 8 weeks. Animals were divided into four groups: normal control, MS control group given saline, MS groups given fenugreek oil (4 ml/kg), and metformin (100 mg/kg) daily for 4 weeks. Blood pressure, heart rate, creatine kinase-MB, and lactate dehydrogenase were estimated. Also renal function and antioxidant activity were evaluated. In addition, to C-reactive protein, and fibrinogen determined.
Results: Fenugreek oil and metformin caused decrease in both MS-induced increase in blood pressure and heart rate. They reduced creatinine, blood urea nitrogen, uric acid, albumin, and MDA with increased Glutathione, and superoxide dismutase. Drugs also decreased C-reactive protein, and fibrinogen compared with MS control group.
Conclusion: Fenugreek oil and metformin ameliorate cardiac and renal complication of MS via their antioxidant activity

Keywords: Metabolic syndrome; fenugreek oil; metformin; antioxidant activity.

1. INTRODUCTION

The prevalence of metabolic syndrome (MS) has increased worldwide mainly due to the obesity epidemic [1]. Although there is no consensus about central mechanism for the pathogenesis of the metabolic syndrome, there are two main features; the visceral obesity and impaired insulin, in particular stand out as potential etiologies underlying the associated abnormalities of MS [2].

Many authorities also recognize metabolic syndrome as a pro-inflammatory and prothrombotic state, in addition fructose feeding induced ventricular dilatation, ventricular hypertrophy, decreased ventricular contractile function, and infiltration of inflammatory cells in heart [3,4].

Substituting the starch carbohydrate content in laboratory rodent diet with fructose resulted in elevated blood pressure within a period of 6-8 weeks. The effects of high fructose feeding have been reported to be concentration and time-dependent [5,6].

Vascular dysfunction due to a fructose-rich diet has been reported in rat, and it is recognized that vascular dysfunction in metabolic syndrome is associated with increased vasoconstrictor sensitivity and production of vascular superoxide anions [7].

It is evident that this state of chronic inflammation may contribute to the chronic illnesses associated with obesity, namely atherosclerosis, dyslipidemia and insulin resistance [8]. Additionally, CRP is emerging as an independent and strong predictor and mediator of cardiovascular diseases [9].

S´anchez-Lozada et al., [10] reported functional changes including elevated plasma creatinine and albuminuria and morphological changes including fatty infiltration and thickening of glomeruli have been reported after 60 days of fructose feeding in rat [11].

Oxygen-derived free radical reactions have been implicated in the pathogenesis of many human diseases/disorders, including cardiovascular disorders, renal disorders and, diabetes [12]. However, nature has endowed each cell with adequate protective mechanisms against any harmful effects of free radicals. Superoxide dismutase (SOD), catalase, glutathione peroxidase, glutathione reductase, thiols, and disulfide bonding are buffering systems in different cells [13].

Plants provide a rich source of antioxidants to overcome the action of ROS as they can reduce free radical formation and scavenge free radicals [14]. Fenugreek (*Trigonella foenum-graecum L. Leguminosae*) is one of the oldest medicinal plants with medicinal properties such as hypocholesterolemic, antibacterial, gastric stimulant, anorexigenic, antidiabetic, galactagogue, hepatoprotective and anticancer. These beneficial effects including the antidiabetic and hypocholesterolemic effects of fenugreek are mainly attributable to the intrinsic dietary fiber constituent which have promising nutraceutical value [15,16].

Metformin is a biguanide agent that is currently used in treatment of diabetes mellitus. Metformin improves insulin sensitivity and decreases insulin resistance, targeting a primary failure in Type 2 diabetes [17]. Metformin suppresses hepatic glucose production and increases glucose utilization, which only occurs in the presence of insulin as metformin enhances insulin action at

the post receptor level in peripheral tissues. The principal site of action of metformin is the liver where it inhibits hepatic glucose production [18,19]

The aim of the study was to investigate the role of fenugreek oil and metformin on MS-induced cardiovascular and renal complications.

2. MATERIALS AND METHODS

2.1 Animals

Twenty four male Sprague Dawley rats weighting 200 to 230 g were used in the current study. They were purchased from the animal house of the National Research Center Institute (Cairo, Egypt). During the study, the animals were housed under conventional laboratory conditions on a 12 hours light/dark cycle and constant temperature (22 ± 1°C).

2.2 Drugs and chemicals

Fenugreek oil was purchased from local herbal store, Haraz (Egypt), Metformin was purchased from Minapharm Pharmaceutical, (Cairo, Egypt). Fructose was purchased from El Nasr Pharmaceutical, (Cairo, Egypt). Heart rate and blood pressure was indirectly measured by non-invasive blood pressure monitor (ML 125 NIBP, AD Instruments, Australia) from the tail of conscious rats by the tail-cuff technique. Albumin, creatinine, blood urea nitrogen (BUN), uric acid, lactate dehydrogenase (LDH), creatine kinase-MB (CK-MB), C-reactive protein (CRP), and fibrinogen kits were purchased from Spectrum Diagnostics, (Obour, Egypt). Glutathione (GSH), MDA, and SOD activity were estimated. Kits were purchased from (Biodiagnostic, Egypt).

2.3 Experimental Design

MS was induced by feeding rats a diet consisting of standard rodent chow in addition to 10% fat, 3% NaCl, and fructose 20% solution in drinking water for 8 weeks according to modified method described by Calvo-Ochoa et al.[20]

Diet and fructose solution were freshly prepared every day. Rats were provided with a high-fructose diet (HFFD) for 8 weeks. Rats were randomly allocated into five groups (six rats each) as follows:

Group 1: normal group received normal laboratory diet, tap water ad libitum and given saline dailyduring the time of experiment.
Group 2: this group fed HFFD for 12 weeks and given saline daily during the time of experiment.
Group 3: this group fed HFFD+fenugreek for 12 weeks and fenugreek oil (4ml/kg) for the last 4 weeks.
Group 4: this group fed HFFD+metformin for 12 weeks and metformin (100 mg/kg) for the last 4 weeks.

At the end of treatment, the animals were fasted for 12 hours weighed and blood samples were withdrawn from the retro-orbital plexus under light anesthesia [21]. Plasma was separated in heparinized tubes by centrifugation at (1,509g, 15 min, 4°C) and divided into small aliquots that were stored for the estimation of the levels of GSH, MDA, and SOD. In addition, The plasma samples were used to estimate the level of creatinine, BUN, uric acid, albumin, LDH, CK-MB, CRP, and fibrinogen. Furthermore systolic blood pressure and heart rate of animals were indirectly measured by the tail-cuff technique, where tail of the animals were warmed for 30 min at 28°C to dilate the tail artery in a thermostatically controlled heating cabinet (Ugo Basille, Italy) for better detection of tail artery pulse, the tail was passed through a miniaturized cuff and tail-cuff sensor that was connected to an amplified pulse was recorded during automatic inflation and deflation of the cuff. An average of at least three measurements was taken on each occasion. Heart rate was recorded automatically by a counter triggered by a pulse wave.

2.4 Biochemical Assays

Plasma sample were used for estimation of the level of creatinine, BUN, uric acid, albumin, LDH, CK-MB, CRP, and fibrinogen.
An aliquot of blood was used for estimating its glutathione (GSH) contents and the other aliquot was centrifuged for separation of plasma and red blood cells for measurement of lipid peroxide content as MDA nmol /ml plasma. The remaining RBCs pellets were used to assess the SOD activity.

2.5 Statistical Analysis

Statistical analysis was performed using (ANOVA) followed by Tukey's post hoc test using SPSS software v21 (SPSS Inc, Chicago, IL). Data were expressed as mean ± standard

deviation (SD) and P values of less than 0.05 were considered as statistically different.

3. RESULTS

During the 8 weeks feeding of HFHFD, normal control rats demonstrated a systolic blood pressure value of 115±1.87 (mm Hg) (Table 2). Maintaining rats on HFHFD for 12 weeks increased systolic blood pressure by 57% compared to normal control (Table 2). Fenugreek oil, and metformin treated groups showed a significant (P<0.05) decrease in systolic blood pressure by 28%, and 26% respectively when compared to MS-induced group.

Rats kept on normal laboratory chow exhibited diastolic blood pressure value of 70±7.69 (mm Hg) (Table 2). Metabolic syndrome was associated with an elevation in diastolic blood pressure level by 36% compared to normal control (Table 2). Fenugreek oil, and metformin treated groups showed a significant (P<0.05) decrease in the levels of diastolic blood pressure by 24%, and 23% respectively when compared to MS-induced group.

Maintaining rats on normal laboratory chow exhibited mean blood pressure value of 85±5.25 (mm Hg) (Table 2). Meanwhile MS-induced rats exhibited a significant increase in mean blood pressure by 45% compared to normal control (Table 2). Administration of fenugreek oil, and metformin under the same condition caused a significant (P<0.05) decrease in mean blood pressure compared to the MS-induced rats by 26 %, 24% respectively.

Normal control rats demonstrated a heart rate value of 309±13.87 (beat/min) (Table 2). Meanwhile, MS-induced rats exhibited an increase in heart rate by 40% compared to normal control (Table 2). Administration of fenugreek oil, and metformin under the same condition caused a significant (P<0.05) decrease in heart rate compared to the MS-induced rats by 60 %, 57% respectively.

Rats kept on normal laboratory chow exhibited total CK-MB value of 101.5±4.32 (U/l) (Table 3). Metabolic syndrome was associated with an elevation in CK-MB level by 210% compared to normal control (Table 3). Fenugreek oil, and metformin treated groups showed a significant (P<0.05) decrease in the levels of CK-MB by 59%, and 55% respectively when compared to MS-induced group.

Maintaining rats on normal laboratory chow exhibited LDH value of 115.67±2.31 (U/l) (Table 3). Meanwhile MS-induced rats exhibited a significant increase in LDH level by 132% compared to normal control (Table 3). Administration of fenugreek oil, and metformin under the same condition caused a significant (P<0.05) decrease in LDH level compared to the MS-induced rats by 67 %, and 66% respectively.

Normal control rats demonstrated a CRP value of 2.77±0.13 (mg/l) (Table 3). Maintaining rats on HFHFD for 12 weeks increased CRP level by 432% compared to normal control (Table 3). Fenugreek oil, and metformin treated groups showed a significant (P<0.05) decrease in the levels of CRP by 82 %, and 81% respectively when compared to MS-induced group.

Rats kept on normal laboratory chow exhibited creatinine value of 0.55±0.02 (mg/dl) (Table 4). Metabolic syndrome was associated with an elevation in creatinine level by 42% compared to normal control (Table 4). Fenugreek oil, and metformin treated groups showed a significant (P<0.05) decrease in the levels of creatinine by 49%, and 26% respectively when compared to MS-induced group.

Maintaining rats on normal laboratory chow exhibited uric acid value of 1.13±0.06 (mg/dl) (Table 4). Meanwhile MS-induced rats exhibited a significant increase in uric acid level by 340% compared to normal control (Table 4). Administration of fenugreek oil, and metformin under the same condition caused a significant (P<0.05) decrease in uric acid level compared to the MS-induced rats by 67 %, and 52% respectively.

Normal control rats demonstrated a BUN value of 17.97±2.44 (mg/dl) (Table 4). Maintaining rats on HFHFD for 12 weeks increased BUN level by 13% compared to normal control (Table 4). Fenugreek oil, and metformin treated groups showed a significant (P<0.05) decrease in the levels of BUN by 25 %, and 19% respectively when compared to MS-induced group.

Rats kept on normal laboratory chow exhibited albumin value of 3.58±0.23 (g/dl) (Table 4). Metabolic syndrome was associated with reduction in albumin level by 15% compared to normal control (Table 4). Fenugreek oil, and metformin treated groups showed a significant (P<0.05) increase in the levels of albumin by 20%, 17% respectively when compared to MS-induced group.

Normal control rats demonstrated a blood fibrinogen value of 227.33 ± 1.63 (mg/dl) (Table 5). MS-induced rats demonstrated an increase in the blood fibrinogen level by 62% compared to normal control (Table 5). Fenugreek oil, and metformin treated groups showed a significant ($P<0.05$) decrease in the levels of fibrinogen by 52%, and 33% respectively when compared to MS-induced group.

Normal control rats demonstrated MDA value of 1.59±0.07 (nmol/ml) (Table 6). Maintaining rats on HFHFD for 12 weeks increased MDA by 214% compared to normal control (Table 6). Fenugreek oil, and metformin treated groups showed a significant ($P<0.05$) decrease in MDA by 75 %, 62% respectively when compared to MS-induced group.

Rats kept on normal laboratory chow exhibited glutathione value of 9.813±0.63 (mg/dl) (Table 6). Metabolic syndrome was associated with a lowered glutathione level by 31% compared to normal control (Table 6). Fenugreek oil, and metformin treated groups showed a significant ($P<0.05$) increase in the levels of glutathione by 364 %, 255% respectively when compared to MS-induced group.

Maintaining rats on normal laboratory chow exhibited SOD value of 11.57±0.51 (U/ml) (Table 6). Meanwhile MS-induced rats exhibited a significant decrease in SOD by 32% compared to normal control (Table 6). Administration of fenugreek oil, and metformin under the same condition caused a significant ($P<0.05$) increase in SOD level compared to the MS-induced rats by 391 %, and 213% respectively.

4. DISCUSSION

In the present study, 8 weeks of feeding rats with HFHFD resulted in metabolic syndrome manifested by elevated oxidative stress, blood pressure and heart rate. HFHFD-fed rats also showed an increase in fibrinogen and CRP associated with changes in kidney function such as hyperuricaemia and albuminuria.

During MS, there is an imbalance in glucose metabolism that generates chronic hyperglycemia, which in turn triggers oxidative stress and causes an inflammatory response that leads to cell damage [22].

It has been suggested that MS is associated with alterations of myocardial metabolism leading to increased myocardial free fatty acids oxidation resulting in lipotoxicity and predisposition to cardiac hypertrophy and dysfunction [23]. The most possible mechanisms for the cardiovascular effect of MS are that it can cause renal sodium retention, increasing cardiac preload. It also activates the renin-angiotensin system, sympathetic nervous system, promotes oxidative stress, and stimulates cardiac fibroblasts, increases heart rate and cardiac overload [24].

The current data revealed that HFHFD caused oxidative stress as shown by marked decrease in GSH, SOD, and increase in MDA. Several studies have reported that MScan cause high production of ROS which may lead to cellular oxidative damage including DNA, lipids, and protein [25].

The results of the present study showed that HFHFD induced kidney dysfunction as indicted by elevation of creatinine, uric acid, BUN, and reduction of albumin levels. Elevated serum uric acid levels are thought to be a potential mechanism linking fructose consumption to MS [26].

The HFHFD in the present work resulted in increase in fibrinogen and CRP level indicting cardiovascular changes. CRP has a role in the modulation of the harmful effect of oxidized LDL on endothelial function, contributing to oxidative stress and the subsequent production of free radicals that may contribute to damage and endothelial dysfunction and to oxidation of the lipoproteins in atherosclerotic lesions [27].

Fibrinogen, an acute-phase reactant like CRP, rises in response to a high cytokine state. Thus, prothrombotic and proinflammatory states may be metabolically interconnected [28].

The administration of fenugreek oil to MS-induced rats provoked a significant reduction of blood pressure associated with reduction of heart rate, LDH, CK-MB and reduction of CRP as well as fibrinogen. Furthermore fenugreek oil improved of renal function and oxidative stress biomarkers.

The administration of fenugreek oil provoked a significant increase in GSH, and SOD, and decrease in MDA level. Free radical scavenging activity of fenugreek is due to phenolic compounds present in the seeds [29].

The administration of fenugreek oil significantly decreased CRP level indicating anti-inflammatory activity. This effect could be exhibited by diosgenin, which was found to attenuate

inflammation and promote differentiation in the adipocytes [30].

The administration of fenugreek oil significantly decreased MS-induced hypertension and heart rate. Previous studies reported that the hypotensive effect of fenugreek was mediated through serotonin antagonism [31]. Recent studies have shown that, diosgenin contained in fenugreek protects vascular function by attenuating aortic calcification, increasing the expression of endothelial NO synthase, and inhibiting differentiation in aortic vascular smooth muscle cells [32,33].

Cardio-protective influence of fenugreek was evidenced by their blocking potential on renin-angiotensin system and nitric oxide metabolites in circulation [34].

Fenugreek also improved the glycogen content and hexokinase activity in muscle and caused a significant reduction in CK-MB isoenzyme activity in serum suggesting the potential protective effects of fenugreek against peripheral tissue damage [35].

In the present study, fenugreek oil improved hyperuricaemia, albuminuria, and kidney function. The results of the present study are in agreement with Konopelniuk et al. [36] who reported that the beneficial effects of fenugreek galactomannan were evidenced by their capacity to inhibit diabetes-induced kidney injury through lowering the urea and creatinine content in plasma. The improvement in kidney dysfunction induced by fenugreek administration could be related to its ability to increase the activities of antioxidants in the kidneys [37].

Furthermore, fenugreek oil administration caused a significant reduction in fibrinogen level leading to improvement of kidney function. Eldin et al. [38] stated that, fenugreek aqueous extract in different concentrations inhibits clot formation and increases prothrombin time. They suggested that, anticoagulant effect of fenugreek may be attributed to several coumarin compounds that have been noted in the seeds.

Euglycemia caused by metformin ameliorated oxidative stress as shown by significant increase in GSH, and SOD, and decrease in MDA level. Furthermore, Correia et al. [39] reported that metformin possessed a direct scavenging effect against oxygenated free radical. They postulated that metformin ameliorated oxidative stress through controlling hyperglycemia induced generation of free radicals. Similarly Obi et al. [40] reported a reduction in serum MDA level and an increase in GSH level after administration of metformin.

The administration of metformin significantly decreased CRP level induced by MS. Hristova, [41] and Zhou et al.[42] reported that metformin in addition to its classical effects on glucose and lipid metabolism, it inhibits low-grade inflammation.

Prevention of MS also protected against cardiovascular damage such as hypertension, heart rate and kidney function alteration. Moreover metformin reduced MS-induced LDH and CK-MB elevation. Several studies have found that in Type 2 diabetic patients, metformin improves vascular function, reduces arterial stiffness, reduces cardiovascular events, improves diastolic function, and left ventricular diastolic dysfunction via increase availability of NO and improves endothelium-dependent vasodilation [43,44].

Likewise Lexis et al. [45] found that metformin treatment reduced CK-MB and troponin-T. This effect could be attributed to that metformin increase glucose utilization of the heart by facilitating glucose metabolism via increase of GLUT-4. Similarly, Kelleni et al. [46] reported that pretreatment with metformin attenuated the rise in CK-MB and LDH.

Metformin could also favor a protection against the deleterious consequences of hyperglycemia in kidney, restoring normal renal function and morphology [47,48]. Study of Takiyama et al. [49] demonstrated that metformin treatment (250 mg/kg/d) during 9 to 39 weeks ameliorates tubular injury associated with hyperglycemia. It has been also demonstrated that metformin prevents gentamicin-induced acute renal failure, presumably by decreasing ROS-mediated lipid peroxidation, and decreases the development of the tubulointerstitial fibrosis during the diabetic nephropathy [50]. Nephroprotective effect of metformin could be attributed to antihyperglycemic, anti- inflammatory and antioxidant effects [51].

In addition, metformin administration caused a significant reduction in fibrinogen level as reported before [52]. In animal model, metformin was found to prolong activated partial thromboplastin and prothrombin time, inhibit PAI-1, and improve endothelial cell damage [53,54].

Table 1. Nutritional composition of diets

Nutrient composition	Normal control	HFFD
Fat (%)	4	14
Carbohydrates (total) (%)	50	50
Fructose (%)	0	20
Maltodextrin 10 (%)	15	15
Protein (%)	22	22

Abbreviation: HFHFD, high-fructose high-fat diet

Table 2. Effect of fenugreek oil, and metformin on blood pressure and heart rate in MS-induced rats

Parameters / Treatment	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)	Mean blood pressure (mm Hg)	Heart rate (beat/min)
Normal control	115±1.87	70±7.69	85±5.25	309±13.87
HFFD	180±7.35#	95±5.47#	123±6.23#	433±9.81#
HFFD + Fenugreek(4ml/kg)	130±1.86#*	130±1.86#*	91±8.06*	174±1.86#*
HFFD + Metformin (100 mg/kg)	133±1.85#*	73±5.68*	93±6.44*	188±1.87#*

Abbreviations:MS, metabolic syndrome. Results are expressed as mean ± SD (n = 6). The statistical comparison of difference between the control and the treated groups were carried out using one-way ANOVA. Relative organ weight = (organ weight/body weight) × 100

**Statistically significant from the MS-induced rats treated with HFHFD only at P < 0.05.*

#Statistically significant from the control values at P < 0.05

Table 3. Effect of fenugreek oil, and metformin on pathophysiological cardiovascular parameters in MS-induced rats

Parameters / Treatment	CK-MB (U/l)	LDH (U/l)	CRP (mg/l)
Normal control	101.5±4.32	115.67±2.31	2.77±0.13
HFFD	315.07±15.15#	268.83±6.24#	14.73±1.64#
HFFD + Fenugreek (4ml/kg)	129.5±3.39#*	129.5±3.39#*	2.66±0.18*
HFFD + Metformin(100 mg/kg)	143.17±4.83#*	92.5±1.87#*	2.78±0.24*

Abbreviations: CK-MB, Creatine kinase-MB; LDH, Lactate dehydrogenase, CRP; C reactive protein; MS, metabolic syndrome. Results are expressed as mean ± SD (n = 6). The statistical comparison of difference between the control and the treated groups were carried out using one-way ANOVA.

**Statistically significant from the MS-induced rats treated with HFHFD only at P < 0.05.*

#Statistically significant from the control values at P < 0.05

Table 4. Effect of fenugreek oil, and metformin on kidney function in MS-induced rats

Parameters / Treatment	Creatinine (mg/dl)	Uric acid (mg/dl)	BUN (mg/dl)	Albumin (g/dl)
Normal control	0.55±0.02	1.13±0.06	17.97±2.44	3.58±0.23
HFFD	0.78±0.03#	4.97±0.11#	20.32±3.6#	3.05±0.14#
HFFD + Fenugreek (4ml/kg)	0.4±0.03#*	1.65±0.13#*	15.24±2.34#*	3.67±0.21*
HFFD + Metformin (100 mg/kg)	0.58±0.03*	2.41±0.11#*	16.46±2.58#*	3.58±0.24*

Abbreviations: BUN; blood urea nitrogen; MS, metabolic syndrome. Results are expressed as mean ± SD (n = 6). The statistical comparison of difference between the control and the treated groups were carried out using one-way ANOVA.

**Statistically significant from the MS-induced rats treated with HFHFD only at P < 0.05*

#Statistically significant from the control values at P < 0.05

Table 5. Effect of fenugreek oil, and metformin on fibrinogen in MS-induced rats

Parameters / Treatment	Fibrinogen (mg/dl)
Normal control	227.33±1.63
HFFD	369.17±7.83#
HFFD + Fenugreek (4ml/kg)	176.33±4.65#*
HFFD + Metformin (100 mg/kg)	247.17±1.47#*

Abbreviations: MS, metabolic syndrome. Results are expressed as mean ± SD (n = 6). The statistical comparison of difference between the control and the treated groups were carried out using one-way ANOVA.

**Statistically significant from the MS-induced rats treated with HFHFD only at P < 0.05.*

#Statistically significant from the control values at P < 0.05.

Table 6. Effect of fenugreek oil, and metformin on oxidative stress paramaters in MS-induced rats

Parameters / Treatment	MDA (nmol/ml)	GSH (mg/dl)	SOD (u/l)
Normal control	1.59±0.07	9.813±0.63	11.57±0.51
HFFD	4.99±0.44#	6.74±0.43#	7.84±0.36#
HFFD + Fenugreek (4ml/kg)	1.27±0.08#*	31.24±0.95#*	38.5±1.8#*
HFFD + Metformin (100 mg/kg)	1.89±0.09#*	23.92±1.58#*	24.5±1.24#*

Abbreviations: MDA, Malondialdehyde; GSH, Glutathione reduced ;SOD, Superoxide Dismutase; MS, metabolic syndrome. Results are expressed as mean ± SD (n = 6). The statistical comparison of difference between the control and the treated groups were carried out using one-way ANOVA.

**Statistically significant from the MS-induced rats treated with HFHFD only at P < 0.05.*

#Statistically significant from the control values at P < 0.05.

5. CONCLUSIONS

In conclusion, 8 weeks of feeding rats with HFHFD resulted in metabolic syndrome. Administration of fenugreek oil or metformin during four weeks in metabolic-sydrome induced rats decreased blood pressure and heart rate, and improved the renal function. The fenugreek oil was more potent than metformin. These effects could be related to antioxidant activity of these compounds.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The experimental design was carried out according to the regulation of ethic committee of faculty of Pharmacy Cairo University.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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