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# Anti-Insulin Resistance Effect of Black Seed (*Nigella sativa*) Extracts In Metabolic Syndrome Induced-Rats

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## Abstract

Metabolic syndrome (MS) is a group of metabolic disorders that includes hypertension, central obesity, insulin resistance, and atherogenic dyslipidemia. It is closely linked to an elevated risk of diabetes and atherosclerotic and non-atherosclerotic cardiovascular disease. In the currentstudy, *Nigella sativa* (NS) ethanolic and aqueous extracts were investigated for their effect on blood glucose level, insulin resistance and lipid profile in MS induced-rats. Metabolic syndrome was induced by fed rats on a high fat diets supplemented with 1 % cholesterol powder and treated with 10 % fructose added to drinking water for 5 weeks. Twenty-four albino male rats (180 ± 5 g) were divided into four groups: group 1 (normal control) was fed on basal diet, group 2 (positive control) treated with high fat diet and 10 % fructose in drinking water (about 25ml daily per rat). Group 3 and group 4 treated with (NS) ethanolic and aqueous extracts (300 mg\kg), respectively, after induction of MS. Levels of glucose, insulin, lipid profile parameters, alanine aminotransaminase (ALT) and aspartate aminotransaminase (AST) were evaluated. Results revealed that at the end of experiment after eighty five days, in a comparison to positive control, both ethanolic and aqueous extracts of (NS) were recorded a significant increase in a high-density lipoprotein-cholesterol (HDL-C) level, accompanied by a significant decrease in levels of glucose, insulin, insulin resistance, (ALT), and (AST).There were no histological alterations in the pancreas after aqueous extract treatment. In conclusion, (NS) could introduce a potential natural therapy against MS.

**Keywords**: Metabolic Syndrome; Type II diabetes mellitus; insulin resistance; hyperlipidemia; *Nigella sativa*; hyperinsulinemia.

## 1. Introduction

Metabolic syndrome (MS) is a group of metabolic disorders that includes hypertension, central obesity, insulin resistance, and atherogenicdyslipidemia, and is closely linked to an elevated risk of diabetes and atherosclerotic and non-atherosclerotic cardiovascular disease (CVD) [1].

Diabetes mellitus is caused by defects in either secretion or action of insulin leading to hyperglycemia. It is considered as the most common metabolic disorder affecting metabolism of carbohydrate, protein, lipids as well as nucleic acid [2]. Insulin dependent diabetes mellitus is known as type I, while non-insulin dependent diabetes mellitus is known as type II. Lifestyle, obesity and hereditary factors are among principal causes of type II diabetes mellitus, in which patients suffer from defected secretion of insulin and developed resistance against insulin in the periphery. Insulin hormone is secreted from beta-cells of pancreatic Langerhans islets.

After its release in blood, it stimulates glucose clearance from blood into different body tissue such as adipose tissue, liver and especially, skeletal muscle [3], and has an essential role in the homeostasis of glucose by controlling its blood level.

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Therapeutics derived from medicinal plants have recently attracted a lot of researchers' interest as more safe medicinal alternatives replacing traditional chemotherapeutics currently used for curing and prophylaxis of different diseases. However, finding potential natural drugs which can effectively deal with type II diabetes mellitus without introducing undesirable side effects remains a challenge to scientists. Many medicinal

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herbals are used for this purpose as they showed anti-hyperglycemic effect and have the advantages of having minimal side effects and low preparation cost.

*Nigella sativa* (NS), Family: Ranunculaceae has been used as a treatment for a variety of health related problems for thousands of years. Anti-histaminic, anti-diabetic, anti-hypertensive, anti-inflammatory, and immune-potentiation are among the pharmacological actions of NS seeds [4]. *Nigella sativa* seed extracts have a strong antioxidant power to avoid or control free radicals, which can cause many modern inflammatory disorders as cancer, diabetes, and coronary artery disease. Because it contains terpenoids, flavonoids, and phenolic chemicals, its traditional use is taken into account [5].

In an experiment conducted on rats, petroleum ether extracts from *Nigella sativa* (NS) have been shown to effectively lower blood lipids and insulin sensitivity [6].

Therefore, (NS) is considered among potential natural sources for alternative therapy against hyperglycemia. The present work aims to investigate the effective anti-insulin resistant and anti-hyperglycemic role of *Nigella sativa* (NS) extracts in metabolic syndrome induced-rats.

## 2. Materials and Methods

### 2.1. Plant material

Black seeds (*Nigella sativa*) were purchased from local market in Cairo, Egypt. Seeds of *Nigella sativa* (NS) were first washed with distilled water, left to dry in shadow and then crushed into powder using electric mechanical grinder(Braun, model 1021, Germany).The final powder was passed through the 40 mesh sieve.

### 2.2. Chemicals

All chemicals, solvents and standards used for identification by HPLC were purchased from Sigma (St. Louis, USA). Highly purified ethanol 99 %, highly purified cholesterol powder, fructose, bile salts and choline chloride were obtained from EL-Nasr Pharmaceutical Chemical Co. (Egypt). Rat Insulin (INS) kits were provided by MyBioSource (Southern California, San Diego, USA).

### 2.3. Preparation of *Nigella sativa* ethanolic extract

Institute (Giza, Egypt). Individual housing was performed in screen-bottomed cages with good aeration at 25 °C and 60 % humidity. Rats were fed on basal diet [10] (Table1) for ten days as an adaptation period.

Petroleum ether was used to defat the prepared *N. sativa* powder using Soxhlet apparatus at a temperature of 40–60 °C. Powder (100 g) maceration was then performed in 0.8 L ethanol (80 %) for 72 h. After filtration, a viscous residue was obtained by concentrating the filtrate under vacuum at 40 °C [٧]. Finally, a black powder was produced after lyophilizing the extract by freeze drying to completely get rid of solvent (Snijders, Tilburg Holland, with vacuum pump) ALUE, pressure (4 x$10^{-2}$ Pa).

### 2.4. Preparation of *Nigella sativa* aqueous extract

The aqueous extract was prepared according to the method described by [٧]. Briefly, Seeds powder was added to hot distilled water in a ratio of 1:10 (100 g in 1 L solvent) and left to boil for 15 min. Then the extract was filtrated through a cloth. A viscous residue was obtained by evaporating to dryness under reduced pressure. The extract was then lyophilized by freeze drying to produce concentrated, aqueous extract in form of powder. (Snijders, Tilburg Holland) with vacuum pump, ALUE, pressure (4 x$10^{-2}$ Pa)

### 2.5. Determination of phenolic acids and flavonoids using HPLC

Samples for identifying phenolic acids and flavonoids were prepared as following the method explained by [8]. Briefly, samples (100 mg/each) were provided with 10 ml of methanol and ultrasonicated for 45 min. Samples were then centrifuged at 2170 RCF for 7 min, supernatants were decanted, filtered using 0.45µm filter and filtrates were kept in vials until analysis.

HPLC was performed by applying a linear gradient at a flow rate of 1.0 ml/min using mobile phase (solvent A: water/acetic acid 98:2 v/v; solvent B: methanol/acetonitrile 50:50 v/v) starting with solvent B at 5 % which gradually increased up to 30 % at 25 min, 40 % at 35 min, 52 % at 40 min, 70 % at 50 min, and 100 % at 55 min. Estimation of phenolic acids and flavonoids was done by plotting a chromatogram at both 280 and330 nm, respectively. Identification and quantification of components were done by comparing peak areas with external standards [9].

### 2.6. Experimental design

A total of twenty-four male albino rats (180 ± 5 g) were obtained from Food Technology Research Animal experiments have been carried out following the guidelines of the National Institute of Health Guide for laboratory animal care and use (NIH Publications No. 8023, revised 1978).

**Table 1: Composition of basal diet and high fat diet**

| Ingredient | Basal diet g/100 g | High fat diet g/100 g |
|---|---|---|
| **Casein** | 15 | 15 |
| **Corn oil** | 10 | 10 |
| **Cellulose** | 5 | 5 |
| **Salt mixture** | 4 | 4 |
| **Vitamin mixture** | 1.0 | 1.0 |
| **Starch** | 65.0 | 53.62 |
| **Sheep tail** | - | 10 |
| **Cholesterol** | - | 1 |
| **Choline chloride** | - | 0.2 |
| **Bile salts** | - | 0.18 |

### 2.7. Induction of metabolic syndrome

After adaptation period, the twenty-four rats were divided into two groups. Group 1 (normal control) composed of six rats fed on basal diet until the end of the experiment. The rest eighteen rats (induction group) were induced to develop metabolic syndrome according to[11] by being fed on high fat diet[12]supplemented with 1 % cholesterol powder and treated with 10 % D-Fructose (99% purity) added to freshly drinking water for 5 weeks. After induction of the metabolic syndrome (confirmed by biochemical analysis),induction group was subdivided into three groups (Group 2 to Group 4 /six rats each). Group 2 (positivecontrol) continued to be fed on the same regime of induction group, i.e., high fat diet supplemented with 1 % cholesterol powder and drinking water (25 ml daily for each rat) supplemented with 10 % fructose until the end of the experiment. Group 3, *Nigella sativa* ethanolic extract (NSEE) was fed for seven weeks on a high fat dietsupplemented with 1 % cholesterol powder, drink water supplemented with 10 % fructose, and in addition, it was orally administrated with ethanolic *N. sativa* extract (300 mg/kg body weight). Group 4, *Nigella sativa* aqueous extract (NSAE) was fed for seven weeks on a high fat diet supplemented with 1 % cholesterol powder and 10% fructose in drinking water and orally administrated with aqueous *N. sativa* extract (300 mg/kg body weight, dissolved in water, 1 ml daily). Table (2) summarizes different experimental rat groups.

**Table 2: Experimental groups**

| Group | Treatment |
|---|---|
| **Group 1 (normal control)** | Basal diet |
| **Group 2 (Positive control)** | HFD+ 10 % fructose**comment 34** |
| **Group 3 (NSEE)** | HFD + 10 % fructose + 1 ml dailyorally administrated with NSEE (300 mg/kg body weight) |
| **Group 4 (NSAE)** | HFD + 10 % fructose +1 ml daily orally administrated with NSAE (300 mg/kg body weight) |

**HFD** High fat diet supplemented with 1% cholesterol **NSEE** ***Nigella sativa*** **ethanolic extract**
**NSAE** ***Nigella sativa*** **aqueous extract**

### 2.8. Blood sampling and biochemical analysis

Blood samples were drawn from rats' eye plexuses using fine capillary glass tubes at day 1, 35 and 85 from the start of experiment. Samples were collected in clean dry glass tubes without any anticoagulant and left at room temperature for 15 min in order to separate serum. After centrifugation at 1550 RCF for 10 min, the clear supernatant was decanted and stored at -20 °C [13]. Estimation of serum levels of total cholesterol, HDL-C, LDL-C, triglycerides, glucose, insulin, ALT, and AST were done in triplicates according to biochemical methods described in [14-18] and the mean values were calculated.

### 2.9. Determination of insulin level and insulin resistance using ELISA

Instructions of manufacturer were followed to estimate insulin level in serum using Rat Insulin (INS) kits, in which a sandwich enzyme-linked immunosorbent assay (ELISA) BiotekElx 800.USA. In a microtiterplate coated with mouse monoclonal anti-rat insulin antibodies. Calculation of insulin resistance was done according to [19] using the homeostasis model assessment index for insulin resistance (HOMA-IR) by applying this equation: HOMA-IR index=[fasting glucose (mmol/L) × fasting insulin (μU/ml)]/22.5

### 2.10. Histopathological analysis of pancreas

All rats participated in the experiment have been scarified by its end (i.e., after eighty-five daysfrom the start of experiment) using diethyl ether. Pancreas was isolated and samples were prepared for microscopical examinations following the method described by [20]. Briefly, the organ was preserved in 10 % neutral formalin solution, embedded and sectioned in paraffin wax, at the thickness of 5.6 μm and eventually eosin and hematoxylin were used for staining.

### 2.11. Statistical analysis

Data from results were presented as means ± S.D and analyzed using a one-way analysis of variance

(ANOVA). Differences between groups were determined using the Duncan test and *p* values of <0.05 were considered significant.[21].

## 3. Results and discussion

### 3.1. Phenolic and flavonoid components

About eight-thousands phenolic compounds are found in nature, over half of which are flavonoids[22]. Our results revealed that phenolic acids in *Nigella sativa* (ethanolic and aqueous extracts) are pyrogallol, gallic, P-OH-benzoic,ferulic, salicylic, p-coumaric and cinnamic acids (Table 3). Ferulic acid is the major phenolic acid in both of the two extracts followed by P-OH- benzoic acid. While, flavonoids in *N. sativa* extracts are found to be naringin, hesperidin, rutin, quercetin, naringenin, hesperetin, kaempferol, apigenin and catechin (Table 4). This is consistent with previous findings reporting that typical constituents of *N. sativa* included pyrogallol, para-hydroxyl benzoic and ferulic acids as well as naringin and quercitrin [23-25]. Furthermore, it has been proved that some phenolic and flavonoid compounds have antioxidant, anti-inflammatory and anticancer activity. Moreover, owing to their active ingredients, *N. sativa* extracts could play an effective role in preventing numerous diseases due to their anti-obesity, hepatoprotective, antibacterial, anti-inflammatory, and neuro-protective effects as well as antidiabetic, gastroprotective and antitumor activities [26-27].

**Table 3: Concentration of phenolic acids (µg/mg on dry weight basis) in different *Nigella sativa* extracts**

| Phenolic acids | NS ethanolic extract (µg/mg) | NS aqueous extract (µg/mg) |
|---|---|---|
| **Pyrogallol** | 0.15 | 0.11 |
| **Gallic** | 0.21 | 0.15 |
| **P-OH- benzoic** | 0.33 | 0.28 |
| **Ferulic** | 0.36 | 0.34 |
| **Salicylic** | 0.16 | 0.19 |
| ***P*-Coumaric** | 0.19 | 0.17 |
| **Cinnamic** | 0.05 | 0.08 |

**Table 4: Flavonoid components (µg/mg on dry weight basis) in different *Nigella sativa* extracts**

| Flavonoid components | NS ethanolic extract (µg/mg) | NS aqueous extract (µg/mg) |
|---|---|---|
| **Naringin** | 0.42 | 0.32 |
| **Hesperidin** | 0.15 | 0.09 |
| **Rutin** | 0.35 | 0.21 |
| **Quercetin** | 0.80 | 0.65 |
| **Naringenin** | 0.29 | 0.22 |
| **Hesperetin** | 0.11 | 0.06 |
| **Kaempferol** | 0.08 | 0.12 |
| **Apigenin** | 0.23 | 0.27 |
| **Catechin** | 0.31 | 0.35 |

### 3.2. Glucose, insulin, and insulin resistance

After induction of metabolic syndrome using high fat diet supplemented with 1 % cholesterol powder and 10% fructose in drinking water, rats in group 2 (positive control) showed a significant increment in serum levels of glucose, insulin, and insulin resistance (expressed by HOMA-IR) comparing with group1 (negative control). (Table5). As seen by the data, using *Nigella sativa* extracts in this study resulted in a significant reduction in glucose level as well as insulin concentration. In addition, insulin resistance (expressed by HOMA-IR) is being decreased.

**Table 5: Glucose, insulin, and insulin resistance in studied groups**

| Group | Glucose (mg/dl) | Insulin (ng/ml) | HOMA-IR |
|---|---|---|---|
| **Group 1 (normal control)** | $84.23^{d}$±3.59 | $1.45^{b}$±0.48 | $14.14^{c}$±3.33 |
| **Group 2 (Positive control)** | $142.43^{a}$±2.9 | $2.54^{a}$±0.46 | $43.07^{a}$±3.64 |
| **Group 3 (NSEE)** | $118.75^{c}$±3.11 | $1.53^{b}$±0.16 | $21.15^{b}$±2.57 |
| **Group 4 (NSAE)** | $132.51^{b}$±4.20 | $1.50^{b}$±0.20 | $23.14^{b}$±3.58 |

The mean valueswith different superscript alphabets in the same column indicate significant differences ($P < 0.05$)
Each value represents the mean ± standard deviation (SD) NSEE *Nigella sativa* ethanolic extract
NSAE *Nigella sativa* aqueous extract HOMA-IR Homeostatic Model Assessment for Insulin Resistance

These findings agree with previous studies [28-31]. Diabetes mellitus type II is suggested to be developed following chronic intake of diets rich in carbohydrates and saturated lipids such as western diet [32]. Substantial intracellular metabolic alterations are known to be induced in liver and other body tissues as a result of diabetes. Insulin resistance is a condition associated with impaired insulin signalling and glucose clearance [33].Chronic fructose consumption induces

downregulation of insulin receptors and increases triglycerides production leading to insulin resistance [34].Our results are in line with previous studies which reported that *Nigella. sativa* extract mixture inhibited liver gluconeogenesis, and hence, could have a potential therapeutic hypoglycemic effect against diabetes mellitus type II [35-36]. Important steps in starch digestion are carried out by pancreatic α-amylase, which results in linear maltose and branched isomaltose oligosaccharides. These oligosaccharides are then subsequently digested by intestinal α-glucosidase, giving absorbable monosaccharides. In this regard, inhibitors of intestinal α-glucosidaseand/or pancreatic α-amylase can effectively slow starch digestion and absorption during the early stages of digestion, resulting in a significant delay in postprandial hyperglycemia and a positive impact on insulin resistance and glycemic index regulation [37]. Thus, it is hypothesized that the hypoglycaemic effect of *Nigella. sativa* seedsis due to an inhibitory effect on pervious digestive enzymes[38].Our data showed that, apigenin, gallic acid, rutin and quercetin from the phenolic acids and flavonoids compounds that have detected in *Nigella. Sativa* extracts. Apigenin and gallic acid have the ability to bind to α-amylase in the pancreas. Both of them can bind to pancreaticα-amylase's active site [39]. In addition, both quercetin and rutin inhibit α-amylase, although in different ways: quercetin inhibition is noncompetitive, whereas rutin inhibition is competitive.[40].**3.3. Lipid profile** After induction of metabolic syndrome, there was a considerable increase in total cholesterol, triglycerides, and low density lipoprotein (LDL-C), as well as a decrease in high density lipoprotein (HDL-C) as shown in Table 6. These obtained data are in harmony with the findings of [41] who explained that, dyslipidemia in metabolic syndrome is characterised by elevated plasma triglycerides, LDL-C, and a high total cholesterol to high-density lipoprotein (HDL-C) ratio, all of which indicate an atherogenic profile. Furthermore, the down-regulation of lipoprotein lipase (LPL) and the vLDL-C receptor in skeletal muscle, together with an increase in adipose tissue LPL activity, suggests a shift in fatty acid metabolism from muscle to adipocytes. This process may play a role in the development of obesity in rats with metabolic syndrome caused by a diet. Another possible reason for elevated serum level of triglycerides is the synthesis of chylomicrons following either increased internal production of triglycerides or increased triglycerides absorption after intake of external diets rich in fats, and hence, increased triglycerides absorption [42]

**Table 6: Lipid profile in studied groups**

| Group | Total Cholesterol (mg/dl) | Triglycerides (mg/dl) | HDL-C (mg/dl) | LDL-C (mg/dl) |
|---|---|---|---|---|
| Group 1 (normal control) | $93.09^{d}$±4.75 | $74.93^{d}$±5.01 | $51.47^{a}$±4.66 | $28.57^{c}$±5.75 |
| Group 2 (Positive control) | $189.23^{a}$±7.15 | $127.79^{a}$±0.79 | $32.73^{c}$±5.06 | $49.08^{a}$±4.09 |
| Group 3 (NSEE) | $100.19^{c}$±1.62 | $104.76^{b}$±3.54 | $41.99^{b}$±2.77 | $37.23^{b}$±3.50 |
| Group 4 (NSAE) | $107.58^{b}$±4.41 | $98.58^{c}$±5.91 | $47.15^{ab}$±3.59 | $40.76^{b}$±3.52 |

The mean values with different superscript alphabets in the same column indicate significant differences ($P < 0.05$)
Each value represents the mean ± standard deviation (SD) NSEE *Nigella sativa* ethanolic extract
NSAE *Nigella sativa* aqueous extract HDL-C High density lipoprotein LDL-C Low density lipoprotein

Abnormalities in lipid and lipoprotein levels are commonly linked with diabetes. Because abnormalities in lipid profiles have been linked to an increased risk of coronary heart disease, ideal diabetes treatment should also improve lipid profile in addition to glucose regulation [43].It was clear that, after administration of *Nigella sativa* ethanolic (NSEE) and aqueous extracts (NSAE), group 3 and group 4, respectively, a significant decrease in serumlevels of total cholesterol, triglycerides and LDL-C. Instead, it is accompanied by a significant increase in HDL-C level comparing with positive group (Table 6).This is consistent with[44] who reported that, the lipid-lowering actions of *Nigella sativa* are due to inhibition of dietary cholesterol absorption, decreased hepatic cholesterol formation, and up-regulation of LDL-C receptors. Overall, evidence from an experimental and clinical investigation suggests that *Nigella sativa* seeds are a promising natural therapy for dyslipidemia patients. According to this work, both of the *Nigella sativa* extracts contained nine flavonoid components which may be responsible for thelipid reduction effect of*Nigella sativa*. Changes in the gut bacteria population are one possible mechanism of action for polyphenols like naringin and naringenin. Polyphenols are both substrates for microbial biochemical processes and modulators

of bacterial development, and have been linked to human disease states such as obesity. Flavonoid aglycones like naringenin and quercetin inhibit the growth of a wide range of gastrointestinal bacteria as much as the corresponding glycosides. These pathways provide a wide variety of possibilities for natural plant products as part of the diet [45].

### 3.4. Liver functions

**Table 7: Liver functionsin studied groups**

| Groups | ALT (IU/L) | AST (IU/L) |
|---|---|---|
| **Group 1 (normal control)** | $21.19^{c}$±1.60 | $50.88^{c}$±2.21 |
| **Group 2 (Positive control)** | $47.19^{a}$±3.85 | $72.63^{a}$±1.95 |
| **Group 3 (NSEE)** | $29.25^{b}$±2.08 | $59.73^{b}$±2.74 |
| **Group 4 (NSAE)** | $30.40^{b}$±1.53 | $50.51^{c}$±2.20 |

ALT Alanine aminotransaminase AST Aspartate aminotransaminase
The mean values with different superscript alphabets in the same column indicate significant differences ($P < 0.05$)
Each value represents the mean ± standard deviation (SD) NSEE *Nigella sativa* ethanolic extract
NSAE *Nigella sativa* aqueous extract

The liver is the body's vital biochemical organ and is responsible for numerous essential functions. Therefore, if the liver gets ill or diseased, the consequences for the body's metabolic system can be dangerous [46].The activities of alanine aminotransaminase (ALT) and aspartate aminotransaminase (AST) were significantly increased after the induction of metabolic syndrome, according to data in Table (7). Excess fat accumulation in the liver may result from fructose-rich diets, leading to fatty liver disease, steatohepatitis, and, eventually, cirrhosis. Obesity can develop from liver fat being transferred into the blood and being taken up by fat cells in other tissues. Excess fat accumulation in the liver may result from fructose-rich diets, leading to fatty liver disease, steatohepatitis, and, eventually, cirrhosis. Obesity can develop from liver fat being transferred into the blood and being taken up by fat cells in other tissues. Additionally, circulating fat has been linked to an increased risk of heart disease, insulin resistance, and type 2diabetes. Excess consumption of fructose may thus be at the root of metabolic syndrome [47].The activities of ALT and AST were reduced significantly compared to positive control group after treatment metabolic syndrome induced-rat with *Nigella sativa*extracts.This is in agreement with [48] who studied the hepato-protectiveeffect of *Nigella sativa* alcoholic extract in rats with D-galactose amine/lipopolysaccharide-induced hepatotoxicity, and observed that *Nigella sativa* extract lowered ALT and AST levels closer to control levels. Almost all research revealed that Nigella sativa has a hypoprotective effect due to some of its constituents, such as monoterpenes and thymoquinone, or phenols, phytosterols, and tocopherols [49-50].

### 3.5. Evaluation of histopathological changes inpancreas

Pancreatic tissue examination using light microscopy (Fig. 1) revealed that in comparison to group 1 (normal control), samples from group 2 (positive control) showed apparent histopathological changes including vacuolization of Langerhans islets cells as well as congested pancreatic blood vessel. However, after treatment with ethanolic extract of *Nigella sativa* (group 3) only some vacuolated epithelial cells lining some pancreatic acini were still observed. Interestingly, treatment with aqueous extract of *N. sativa* (group 4) could effectively return the pancreatic tissue to its normal morphological state with no histopathological changes.

## 4. Conclusion

Both ethanolic and aqueous extracts of (*Nigella sativa*) have been shown to ameliorate biochemical and histopathological alterations produced by the metabolic syndrome-inducing high fat/high carbohydrate diet. After oral administration, the plant extracts were found to have hypoglycemic effect, lowering serum levels of glucose, insulin, triglycerides, total cholesterol, and bad LDL-C while elevating good HDL-C. It also has a beneficial influence on liver function. Insulin resistance was lowered as well, as evidenced by the HOMA-IR index. As a result, *Nigella sativa* extracts could be a natural additive therapy for the treatment and prevention of metabolic syndrome.

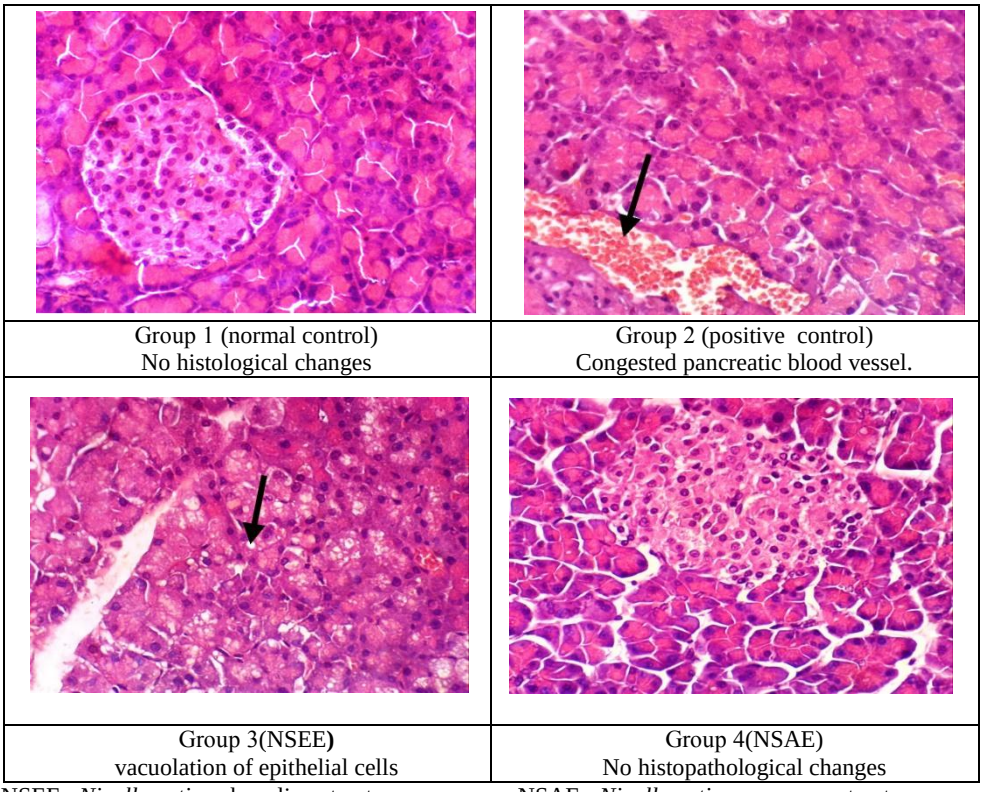


**Fig (1): Histopathological changes of pancreas in studied groups**.

**Conflicts of interest**"
There are no conflicts to declare"

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**الملخص العربي**

## تأثير مستخلصات حبة البركة (*Nigellasativa*) علي مقاومة الأنسولين في الفئران المصابة بمتلازمة التمثيل الغذائي

متلازمة التمثيل الغذائيهي مجموعة من الاضطرابات الأيضية التي تشمل ارتفاع ضغط الدم ، السمنة المركزية ، مقاومة الأنسولين ،خلل في مستوى الدهون في الدم ، ترتبط متلازمة التمثيل الغذائي ارتباطًا وثيقًا بزيادة خطر الإصابة بمرض السكري وتصلب الشرايين وأمراض القلب والأوعية الدموية.وقد تم فيهذه الدراسة ،فحص تأثير مستخلصات حبة البركة علىمستوى السكر في الدم ومقاومة الأنسولين ومستوى الدهون في الفئران التي تسببها متلازمة التمثيل الغذائي.لذا فقد تم تقسيم ٢٤ من ذكور الجرذان البيضاء (١٨٠ ± ٥ جم) إلى ٤مجموعات: المجموعة ١ (المجموعة الضابطة) التي تتغذى على الوجبة القياسية، المجموعة ٢ (المجموعة المصابة) التي تم معاملتها بوجبةعالية الدهون و ١٠٪ من الفركتوز في مياه الشرب. بينما المجموعتين٣ و ٤فقد استخدم في تغذيتها المستخلصات الايثانولية والمائية لبذورحبة البركة على التوالي (٣٠٠ مجم / كجم).ثم تم تقييم مستويات الجلوكوز والأنسولين ومستوى الدهون وانزيمات الكبد في نهاية التجربة.وبنهاية التجربةوبالمقارنة مع المجموعة المصابة ، سجلت كل من المستخلصات الإيثانولية والمائية لبذورحبة البركة زيادة معنوية في مستوى البروتين الدهني عالي الكثافة بالإضافة الى إنخفاض معنوي في مستويات الجلوكوز والأنسولين ومقاومة الأنسولين وانزيمات الكبد).ولم يلاحظ وجود أي تغييرات نسيجية في البنكرياس بعد المعاملة بالمستخلص المائي،وبذلكيمكن استنتاج أن المستخلصات الايثانولية والمائية لبذورحبة البركة يمكن ان تكون وسيلة طبيعيةمساعدة في حالات اضطرابات متلازمة التمثيل الغذائي.

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