
***EFFECT OF SOME LEVELS FROM NIGELLA SATIVA AS SEEDS OR
WATER EXTRACT ON RATS SUFFERING FROM
HYPERLIPIDEMIA AND DIABETES.***

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EFFECT OF SOME LEVELS FROM NIGELLA SATIVA AS SEEDS OR WATER EXTRACT ON RATS SUFFERING FROM HYPERLIPIDEMIA AND DIABETES.

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Abstract

Objective: The main target of this study was to investigate the effect of diets supplemented with three levels from *Nigella sativa* seeds (2.5, 5 and 10%) or water extract of *Nigella sativa* seeds in drinking water (2.5%, 5% and 10% W/V) on serum glucose, lipid profile, kidney functions and liver enzymes in addition to nutrition evaluation of rats suffering from hyperlipidemia and diabetes.

Material & Methods: The experiment was carried out using 48 male albino rats (Sprague Dawley strain) weighting 130 ± 5 g. The rats were divided into two main groups. The first main group (n = 6) fed on basal diet as negative control. The second main group (n = 42) fed on hyperlipidemic diet for 6 week to induce hyperlipidemia, after this period, the second main group injected with (150 mg aloxane / kg body weight) to induce hyperglycemia. The rats in the second main group were randomly divided into seven subgroups as a following: *Subgroup (1)* fed on hyperlipidemic diet as a positive control group. *Subgroups (2, 3 and 4)* fed on hyperlipidemic diet containing 2.5%, 5% and 10% *Nigella sativa* seeds, respectively. *Subgroups (5, 6 and 7)* fed on hyperlipidemic diet and treated daily with extract of *Nigella sativa* seeds in drinking water (2.5%, 5% and 10% W/V), respectively. All groups were kept feeding on experimental diets for 28 days.

Results: The results indicated that, hyperlipidemia and hyperglycemia increased serum glucose, kidney functions, liver enzymes and lipid profile, significantly, except HDL-c., as compared to healthy rats. Treating rats which were suffering from hyperlipidemia and hyperglycemia with different levels from *Nigella sativa* seeds or water extract prepared from different levels from *Nigella sativa* led to a

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general improvement in health of rats, especially when used high level from seeds or water extract.

Conclusion: It was finally concluded that, treated rats which suffer from hyperlipidemia and hyperglycemia with *Nigella sativa* seeds or water extract prepared from *Nigella sativa* seeds, especially when used high levels from seeds or extraction, could be implemented in the treatment of hyperlipidemic subjects suffering from diabetes.

Key words: *Hyperlipidemia, diabetes, rats, Nigella sativa, glucose, lipid profiles, kidney functions and liver enzymes.*

EFFECT OF SOME LEVELS FROM NIGELLA SATIVA AS SEEDS OR WATER EXTRACT ON RATS SUFFERING FROM HYPERLIPIDEMIA AND DIABETES.

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Introduction:

Hyperlipidemia, being an important risk factor for cardiovascular disease, is a serious public health problem in the world. Its major role in the pathogenesis of atherosclerosis has been implicated by several clinical and epidemiological studies (*Jaffar et al., 2004*). Hyperlipidemia also has an indirect role by stimulating the production of oxygen free radicals (OFRs) from polymorphonuclear leukocytes (PMNLs) and monocytes (*Prasad, 2005*). Regarding its treatment, nowadays there is an increasing interest toward the potential health benefits of medicinal plants.

Diabetes Mellitus (DM) is one of the most common metabolic disorders, with a worldwide prevalence estimated to be between 1 % and 5 %. The increasing prevalence of DM in the world is a cause for concern. DM leads to abnormalities in carbohydrate, protein and lipid metabolism and increases the risk of developing atherosclerotic arterial disease by two- to six folds (*Sacks, 1997*).

Interest in medicinal plants has burgeoned due to increased efficiency of new plant- derived drugs and the growing interest in natural products. Because of the concerns about the side effects of conventional medicine, the use of natural products as an alternative to conventional treatment in healing and treatment of various diseases has been on the rise in the last few decades (*Dattner, 2003 and Fong, 2002*).

The use of alternative medicine (AM) has increased recently and attracted the attention of many researchers all over the world. This interest has been accentuated by a concern that such treatment may be harmful to the patients despite their apparent innocuousness (*Hunt et al., 2000*).

Nigella sativa Linn (*N. sativa*) commonly known as black seed or black cumin, is an annual herb from the botanical family of Ranunculaceae. The seeds of the plant have been used in the Southeast Asia, Middle and Far East

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as a natural remedy to treat many diseases, including asthma, hypertension, diabetes, hypercholesterolemia, inflammation, arthritis, tumor, gastrointestinal disturbances and gynecological disorders for over 2000 years (*Ali and Blunden, 2003; El-Din et al., 2006; Ramadan, 2007*). They are extensively used as spice, condiment and aromatic which can be added to tea, coffee, casseroles or breads. The ground seed can be mixed with honey or sprinkled on salads (*Ramadan, 2007*).

The seed of *N. sativa* has over 100 different chemical components, including mucilage, crude fiber, reducing sugars, resins, alkaloids, flavonoids, organic acids, sterols, tannins and saponins, in addition to the high content of unsaturated fatty acids, especially linoleic acid (18:2 □-6) and oleic acid (18:1 □-9) and proteins. It also has yellowish volatile (essential) oil (*Akram, 1999 and Gilani et al., 2004*). It is known that the biological activity of *N. sativa* seeds is attributed to its essential oil components (*Hajhashemi et al., 2004*). The main compounds contained are thymoquinone (30 - 48%), p-cymene (7 - 15%), carvacrol (6 - 12%), 4-terpineol (2 - 7%), t-anethole (1 - 4%) and a sesquiterpene longifolene (1 - 8%) (*Burits and Bucar, 2000*) in which thymoquinone (TQ) and its derivatives [dithymoquinone (DTQ), thymohydroquinone (THQ) and thymol (THY)] are the most putative pharmacologically active constituents of *N. sativa* (*Padhye et al., 2008*).

The main target of the present investigation is to study the influence of *Nigella Sativa* L as a Seeds or water extract on serum glucose, lipid profile, kidney functions and liver enzymes of rats suffering from hyperlipidemia and diabetes.

Materials and Methods:

Materials:

Casein, all minerals, vitamins, cellulose, choline chloride and alloxan were obtained from El-Gomhoria Company, Cairo, Egypt.

Nigella Sativa Linn (seeds) was purchased from Field Crops Research Institute, Agricultural Research Centre, Ministry of Agriculture Cairo, Egypt.

Normal male albino rats (48) Sprague Dawley Strain weighing (130 ± 5 g) obtained from Helwan farm, Cairo, Egypt.

Corn oil, corn starch and vegetable ghee were obtained from local market.

Methods:

Preparation of Extract

An extract of *N. sativa* L. seeds was prepared using the method described by **Farida et al. (1987)**. Briefly, *N. sativa* L. seeds were purchased from a local herb store. An extract of *N. sativa* L. seeds in drinking water (5 %) was prepared fresh daily by boiling the seeds (50 g) in drinking water (1000 ml) for 10 min and then filtering through 4 layers of surgical gauze to obtain the water extract used for the experiment.

In this study, extractions of *N. sativa* L. seeds were prepared by using 2.5%, 5% and 10%.

Biological Study:

Male albino Sprague Dawley rats (48 rats weighed 130±5 g) were housed in wire cages in a room maintained at 25 ± 2° C in the animal house of the Faculty of Home Economics, Helwan University . The animals were kept under normal healthy conditions and fed basal diet for one week (adaptation period). The basal diet consisted of protein 14% (as casein), corn oil 4%, choline chloride 0.2%, vitamin mixture 1%, salt mixture 3.5%, fiber 5% and the remainder was corn starch (**Reeves et al., 1993**), water was provided ad libitum. After the adaptation period, the rats were divided into two main groups. The first group (n = 6) was fed basal diet as negative control (healthy rats). The second main group (n = 42) fed on diet containing (casein 14%; Choline chloride 0.20%; vitamin mixture 1.0%; salt mixture 3.5%; fibers 5%; L-Cystine 0.18%, sucrose 10%, 20% fat (19% saturated fat + 1% unsaturated fat), bile salts (0.25%) and the remainder was corn starch. to induced hyperlipidemia in rats as described by (**Cara et al., 1991**), after this period, lipid fractions were determined in normal and hyperlipidemic groups to insure the induction of hyperlipidemia, then the second main group was injected with aloxane (150 mg / kg body weight) to induce hyperglycemia after fasting overnight (**Buko et al., 1996**). The second main group was randomly divided into seven subgroups according to the following:

- *Subgroup one:* Fed on hyperlipidemic diet (positive control).
- *Subgroup two:* Fed on hyperlipidemic diet containing 2.5% *Nigella Sativa* seeds.
- *Subgroup three:* Fed on hyperlipidemic diet containing 5% *Nigella Sativa* seeds.

- *Subgroup four*: Fed on hyperlipidemic diet containing 10% *Nigella Sativa* seeds.
- *Subgroup five*: Fed on hyperlipidemic diet, and treated daily with extract of *N. sativa* L. seeds in drinking water (2.5% W/V) 25g *Nigella Sativa* seeds/ 1000 ml water.
- *Subgroup six*: Fed on hyperlipidemic diet, and treated daily with extract of *N. sativa* L. seeds in drinking water (5% W/V) 50g *Nigella Sativa* seeds/ 1000 ml water.
- *Subgroup seven*: Fed on hyperlipidemic diet, and treated daily with extract of *N. sativa* L. seeds in drinking water (10% W/V) 100g *Nigella Sativa* seeds/ 1000 ml water.

During the experimental period (28 days), the diets consumed and body weights were recorded twice weekly. Biological evaluation for different groups was carried out by determination of food intake, body weight gain% (BWG %) and kidney weight/body weight% according to **Chapman et al., (1959)**.

At the end of the experiment, the rats were fasted overnight, and then the rats were anaesthetized and sacrificed. Blood samples were collected from the aorta. The blood samples were centrifuged and serum was separated to estimate some biochemical parameters, i.e. serum glucose according to **(Tinder 1959)** total cholesterol **(Allain et al, 1974)**, triglycerides **(Fossati and prenape, 1982)**, high-density lipoprotein cholesterol (HDL-C) **(Lopes-Virella et al., 1977)**. While serum low-density lipoprotein cholesterol (LDL-C) and very low- density lipoprotein cholesterol (VLDL-C) were calculated according to the equation of **Friedwald et al. (1972)**. Serum samples were also used for determination of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities **(Reitman and Frankel 1957)**, Uric acid **(Fossati et al., 1980)**, urea nitrogen **(Patton and Crouch, 1977)** and creatinine **(Henry, 1974)**.

The data obtained was analyzed statistically for standard deviation and one-way ANOVA test **(Steel and Torri, 1980)**.

Results And discussion:

Effect of Some Levels from Nigella Sativa as Seeds or Water Extract on Food Intake, Body Weight Gain % and Liver weight /body weight% of Rats Suffering from Hyperlipidemia and Diabetes.

The effect of different levels from *Nigella sativa* seeds and water extract prepared from some levels from these seeds on food intake (g/day), body weight gain % and liver weight / body weight% of rats suffering from hyperlipidemia and diabetes presented in table (1).

The mean value of food intake (g/day/ each rat) of the control positive group decreased than that of the negative control group (12.323 vs. 15.633g), respectively. Food intake of all treated groups with the different levels of seeds or water extract increased, than that of the positive control group.

The highest increase in the mean value of food intake recorded for the group which treated with water extract of *Nigella sativa* seeds (50g seeds/1000 ml water), followed by the group treated with water extract of *Nigella sativa* seeds (100g seeds/1000 ml water), respectively.

Body weight gain % of rats suffering from hyperlipidemia and hyperglycemia (control positive group) decreased significantly $p < 0.05$, as compared to healthy rats (control negative group). The mean values of body weight gain % of the groups treated with low levels from *Nigella sativa* seeds or water extract showed non-significant changes, while the other treated groups recorded significant increase $p < 0.05$, as compared to the positive control group.

Data presented in this table revealed that, non-significant difference in body weight gain % was observed in the groups treated with medium and high levels from *Nigella sativa* seeds or water extract, as compared to the negative control group.

The mean value of liver weight / body weight % increased significantly in the positive control group, as compared to the negative control group. All treated groups which were suffering from hyperlipidemia and diabetes with the three levels from (*Nigella sativa* seeds or water extract) showed significant decrease, as compared to the positive control group, except group of rats which treated with hyperlipidemic diet containing 2.5% *Nigella sativa* seeds.

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The highest decrease in the percent of this organ recorded for the groups treated with water extract prepared from of (10% and 5% *N. sativa*), respectively.

Table (1): Effect of Some Levels from Nigella Sativa as a Seeds or Water Extract on Food Intake, Body Weight Gain % and Liver weight /body weight% of Rats Suffering from Hyperlipidemia and Diabetes.

Groups	Parameters	Food Intake (g/day/rat)	Body weight %	Liver weight / body weight%
Control (-ve)		15.633	38.656 ^a ± 1.981	3.008 ^{d e} ± 0.190
Control (+ve)		12.323	31.609 ^c ± 1.512	3.934 ^a ± 0.172
2.5% <i>N. sativa</i> seed		13.551	33.552 ^c ± 1.636	3.817 ^{a b} ± 0.198
5% <i>N. sativa</i> seed		13.860	36.588 ^{a b} ± 2.128	3.556 ^{b c} ± 0.132
10% <i>N. sativa</i> seed		13.800	37.065 ^a ± 2.243	3.286 ^{c d} ± 0.079
Water extract of <i>N. sativa</i> (2.5%)		13.692	34.006 ^{b c} ± 1.931	3.527 ^{b c} ± 0.411
Water extract of <i>N. sativa</i> (5%)		14.210	37.673 ^a ± 2.437	3.096 ^{d e} ± 0.375
Water extract of <i>N. sativa</i> (10%)		14.00	38.166 ^a ± 3.166	2.851 ^c ± 0.437

LSD: Least significant differences (P<0.05) Mean values in each column with same letters are not significantly different.

Effect of Some Levels from Nigella Sativa as Seeds or Water Extract on Lipid Profile of Rats Suffering from Hyperlipidemia and Diabetes.

Finding in tables (2) presented the effect of Nigella sativa as a seeds or water extract on total cholesterol, triglycerides, high density lipoprotein (HDL-c), low and very low density lipoprotein (LDL-c and VLDL-c) of serum rats suffering from hyperlipidemia and diabetes.

The mean values of serum cholesterol, triglycerides, LDL-c and VLDL-c (mg/dl) increased significantly at $p < 0.05$, whereas, the mean value of serum HDL-c decreased significantly in the positive control group in comparison with the negative control group.

Feeding rats, which were, suffer from hyperlipidemia and diabetes on hyperlipidemic diet containing (2.5%, 5% and 10% *Nigella sativa*) or feeding rats on hyperlipidemic diet and treating with water extract prepared from 2.5%, 5% and 10% *Nigella sativa* (W/V) enhanced the mean values of serum lipid fractions, particularly, with high level of seeds or water extract.

Table (2): Effect of Some Levels from *Nigella Sativa* as a Seeds or Water Extract on Lipid Profile of Rats Suffering from Hyperlipidemia and Diabetes.

Parameters Groups	mg/dl				
	Ch.	TG	HDL-c	LDL-c	VLDL-c
Control (-ve)	85.691 ^g ± 5.179	38.681 ^f ± 4.552	49.190 ^a ± 4.104	28.765 ^h ± 0.619	7.736 ^f ± 0.910
Control (+ve)	186.616 ^a ± 7.645	90.791 ^a ± 5.151	25.335 ^e ± 2.542	143.122 ^a ± 4.266	18.158 ^a ± 1.030
2.5% <i>N. sativa</i> seed	162.666 ^{bc} ± 6.408	74.166 ^{bc} ± 4.956	32.000 ^d ± 3.485	115.833 ^c ± 2.970	14.833 ^{bc} ± 0.991
5% <i>N. sativa</i> seed	148.643 ^{de} ± 7.185	68.095 ^c ± 5.780	35.394 ^{cd} ± 3.485	99.630 ^e ± 3.155	13.618 ^c ± 1.156
10% <i>N. sativa</i> seed	125.768 ^f ± 8.412	53.732 ^e ± 4.399	42.105 ^b ± 4.522	72.917 ^g ± 4.356	10.746 ^e ± 0.879
Water extract of <i>N. sativa</i> (2.5%)	168.455 ^b ± 7.704	78.921 ^b ± 6.681	31.052 ^d ± 3.246	121.618 ^b ± 3.151	15.784 ^b ± 1.336
Water extract of <i>N. sativa</i> (5%)	155.811 ^{cd} ± 6.302	71.000 ^c ± 5.099	32.666 ^d ± 3.669	108.944 ^d ± 3.771	14.200 ^c ± 1.019
Water extract of <i>N. sativa</i> (10%)	142.333 ^e ± 4.179	61.000 ^d ± 5.403	38.833 ^{bc} ± 3.669	91.300 ^f ± 1.532	12.200 ^d ± 1.080

Ch: Cholesterol *TG:* Triglycerides *HDL-c:* High density lipoprotein-cholesterol
LDL-c: Low density lipoprotein-cholesterol *VLDL-c:* Very low density lipoprotein-cholesterol
LSD: Least significant differences ($P < 0.05$) Mean values in each column with same letters are not significantly different.

The mean values of serum cholesterol, triglyceride's, LDL-c and VLDL-c decreased gradually with increasing the levels of *Nigella sativa* seeds or water extract, while HDL-c increased gradually.

Table (2) revealed that, the group of rats which suffer from hyperlipidemia and diabetes and fed on hyperlipidemic diet containing 10% *Nigella sativa* seeds recorded significant decrease $p < 0.05$ in cholesterol, triglycerides, LDL-c and VLDL-c by about 32.605%, 40.817%, 49.052% and 40.819%, respectively, while HDL-c increased by about 66.193%, as compared to the positive control group. On the other hand, treating rats with the high concentration of water extract which prepared from 10% *Nigella sativa* recorded significant decrease $p < 0.05$ in cholesterol, triglycerides, LDL-c and VLDL-c by about 23.769%, 32.812%, 36.208% and 32.812%, respectively, while HDL-c increased by about 53.278%, as compared to the positive control group.

From these results it could be concluded that, *Nigella sativa* seeds or water extract prepared from this seeds improved the lipid profile in rats suffering from hyperlipidemia and diabetes. In this respect, the seeds of *Nigella sativa* plant have been used to promote health and fight disease for centuries especially in the Middle East and Southeast Asia. In South Asia, it is called Kalonji, its Arabic name is Habat-ul-Sauda and its English name is black cumin. This plant has been a great focus of research and has several traditional uses and consequently has been extensively studied for its chemical constituents and biological activities. A lot of animal studies have already been done to determine the various activities of *Nigella sativa* oil on different components of the metabolic syndrome for example blood sugar (*Bamosa, 1997*).

As an aromatic plant, black cumin (*Nigella sativa*) is widely grown in different parts of the world and the seeds of black cumin have been used to promote health for countries especially in the Middle East and Southeast Asia. Black cumin seeds have been widely used in traditional medicine as diuretic and antihypertensive (*Zaoui et al., 2000*), digestive and appetite stimulant (*Gilani et al., 2004*), antibacterial agents (*Ferdous et al., 1992 and El-Kamali et al., 1998*) antidiabetic (*Meral et al., 2001*), renal protective (*Badary et al., 2000*) and possessing antioxidant properties (*Mansour et al., 2002*).

Bahram et al., (2009) reported that, dietary black seed can favorably decrease serum lipid profile and lipid peroxidation levels in hyperlipidemic

rabbits, therefore, it may be considered as a useful therapy for hyperlipidemia. Also *Najmi et al., (2008)* reported that, *Nigella sativa* oil is effective as an add-on therapy in patients with metabolic syndrome. *Nigella sativa* oil has a significant therapeutic activity in diabetic and dyslipidemic patients.

Muhammad and Muhammad (2007) reported that, *Nigella sativa* seeds in the diet have a favorable effect on lipid profile by lowering the triglyceride, total cholesterol and LDL cholesterol and increasing the HDL cholesterol in albino rats.

Nutritional supplementation can enhance the immune response in elderly humans by changing both the total amount and the type of dietary lipids (*Hummell, 1993*). *N. sativa* oil is rich in the n-6 PUFA a-linoleic acid (18:3n-6), the n-3 PUFA a-linolenic acid (18:3n-3), and a small amount of stearidonic acid (18:4n-3) (*Laakso and Voutilainen 1996*). The composition of the seeds reflects the recommended optimal dietary intake of n-3 and n-6 fatty acids, i.e., it has a ratio of n-3 to n-6 fatty acids of 1 to 4 or 5 (*Yehuda and Carasso, 1993*). Dietary supplementation with the *N. sativa* oil has found to improve the immune response of healthy elderly subjects, which is mediated by a change in the factors closely associated with T cell activation (*Wu et al., 1999*).

Indeed, in consistent with our results, the study of *Zaoui et al., (2002)* indicated that oral treatment with *N. sativa* oil, decreased serum cholesterol and TG levels by 15.5 and 22% in normal rats.

In another study, *N. sativa* oil administration to rats significantly decreased serum TC, LDL.C and TG and increased HDL.C (*El-Dakhakhny et al., 2000*).

Le et al. (2004) reported a significant decrease in plasma TG and an increase in HDL.C levels in black seed extract-oral treated rats, compared to the control group. Moreover, a significant reduction was observed in serum TC and LDL.C of patients with mild hypertension after 8 weeks of black seed extract oral administration (*Dehkordi and Kamkhah, 2008*).

The results of *Bamosa et al. (2002)* demonstrated a decrease in serum TC, LDL.C, HDL.C and TG during intraperitoneal injection of thymoquinone in rats. Furthermore, the hypotriglyceridemic effect of nigellamines (that is black seed diterpene alkaloids) was reported in an *in vitro* study, equivalent to the hypolipidemic agent, clofibrate (*Morikawa et al., 2004*).

The hypolipidemic effect of black seed does not seem to be due only to one component, but rather to the synergistic action of its different constituents, including TQ and nigellamine as mentioned above, soluble fiber (e.g. mucilage), sterols, flavonoids and high content of polyunsaturated fatty acids (PUFAs) (*Ali and Blunden, 2003*).

Mechanism of hypolipidemic action of TQ is not fully understood; however, decreased cholesterol synthesis, and more importantly, its antioxidant role have been proposed. Lipid lowering effects of dietary soluble fibers (*Brown et al., 1999 and Talati et al., 2009*) and sterols (*Jones, 1999 and Moruisi et al., 2006*) are probably related to decreased dietary cholesterol absorption, increased primary bile acid synthesis and its fecal losses. Flavonoids may act by making liver cells more efficient to remove LDL.C from blood. To do this, flavonoids increase LDL receptor densities in liver and by binding to apolipoprotein B (*El-Beshbishy et al., 2006 and Weggemans and Trautwein, 2003*).

Effect of Some Levels from Nigella Sativa as Seeds or Water Extract on kidney functions of Rats Suffering from Hyperlipidemia and Diabetes.

Table (3) presented the effect of different levels from (*Nigella Sativa* or water extract) on kidney functions (mg/dl), including (uric acid, urea nitrogen and creatinine) of rats suffering from hyperlipidemia and diabetes.

Data presented in table (3) observed that, values of uric acid, urea nitrogen and creatinine (mg/dl) for control positive group showed a significant increase $p < 0.05$, as compared to the control negative group.

Feeding groups which were suffering from hyperlipidemia and diabetes on hyperlipidemic diet containing different levels from (*Nigella sativa*) showed significant reduction in the mean values of uric acid and urea nitrogen and creatinine at ($p < 0.05$), compared with the positive control group. The same trend was observed when used the different concentrations of water extracts prepared from 2.5%, 5% and 10% *Nigella sativa*.

Table (3): Effect of Some Levels from *Nigella Sativa* as Seeds or Water Extract on Kidney Function of Rats Suffering from Hyperlipidemia and Diabetes.

Parameters Groups	mg/dl		
	Uric acid	Urea nitrogen	Creatinine
Control (-ve)	1.642 ^g ± 0.135	28.120 ^g ± 2.536	0.546 ^f ± 0.083
Control (+ve)	2.495 ^a ± 0.119	77.242 ^a ± 4.778	1.370 ^a ± 0.101
2.5% <i>N. sativa</i> seed	2.124 ^b ± 0.076	68.641 ^b ± 2.574	1.121 ^{b c} ± 0.081
5% <i>N. sativa</i> seed	1.902 ^d ± 0.088	58.169 ^d ± 3.678	0.933 ^d ± 0.080
10% <i>N. sativa</i> seed	1.756 ^f ± 0.058	42.625 ^f ± 1.896	0.771 ^e ± 0.072
Water extract of <i>N. sativa</i> (2.5%)	2.213 ^b ± 0.039	71.000 ^b ± 3.162	1.208 ^b ± 0.041
Water extract of <i>N. sativa</i> (5%)	2.012 ^c ± 0.100	64.666 ^c ± 3.386	1.050 ^c ± 0.082
Water extract of <i>N. sativa</i> (10%)	1.889 ^e ± 0.027	50.333 ^e ± 2.160	0.897 ^d ± 0.033

LSD: Least significant differences ($P < 0.05$) Mean values in each column with same letters are not significantly different.

The mean values of serum uric acid, urea nitrogen and creatinine decreased gradually with increasing the levels of (*Nigella sativa* seeds and water extract of *Nigella sativa*). The lowest mean values of serum uric acid, urea nitrogen and creatinine recorded for the group which treated with the high level from *Nigella sativa* seeds (10 g/100 g diet), followed by the group treated with water extract with the high concentration.

Serum uric acid, urea nitrogen and creatinine decreased by about (29.619%, 99.448 and 43.722%) and (24.288%, 34.837% and 34.525%) in the groups which treated with 10% *Nigella sativa* seeds and water extract of *Nigella sativa* (10%), respectively.

From these results it could be concluded that, *Nigella sativa* seeds or water extract prepared from this seeds improved kidney functions of rats suffering from hyperlipidemia and diabetes.

N. sativa is an annual herbaceous plant that belongs to the family (Ranunculaceae) (*Abdaziz and Kandeel, 2011 and Tajk et al., 2008*). It contains carbohydrates, proteins, (*AbdEl-Aleem and El-Deeb, 2006*), linoleic, oleic and palmitic acid (*Atta, 2003*) and high concentrations of thymoquinone (TQ) and thymol (*Al-Saleh et al., 2006*).

Thymoquinone TQ inhibits nuclear factor-kappaB "NF-kB" (*Sayed and Morcos, 2007*). It may be a clinically valuable agent in the prevention of renal disease (*Sayed-Ahmed and Nagi, 2007*). In this respect, *Ali, (2004)* reported that, in gentamicine induced toxicity, treatment with *N. sativa* oil produced a dose-dependent amelioration of the biochemical and histological indices of nephrotoxicity, coincided with the increase in the scavenger defense system, including GSH concentration and the total anti-oxidant status in renal cortex.

Modern toxicological studies have demonstrated that crude extracts of the seeds and some of its active constituents (volatile oil, TQ) might have a protective effect against nephrotoxicity and hepatotoxicity induced by either disease or chemicals (*Ali and Blunden 2003*).

Effect of Some Levels from Nigella Sativa as Seeds or Water Extract on Serum Glucose and Liver Enzymes of Rats Suffering from Hyperlipidemia and Diabetes.

Finding in tables (4) presented the effect of three levels (2.5%, 5% and 10%) from *Nigella Sativa* seeds and the three concentrations from water extract prepared from (25g, 50g and 100g *Nigella Sativa* seeds / 1000 ml water) on serum glucose and AST and ALT enzymes of rats suffering from hyperlipidemia and diabetes.

Feeding rats on hyperlipidemic diet and treated with (150mg alloxan/kg body weight) induced significant increase $p < 0.05$ in serum glucose and liver enzymes (AST & ALT), as compared to healthy rats fed on basal diet.

Treating rats which were suffering from hyperlipidemia and hyperglycemia with different levels from *Nigella Sativa* seeds or water extract prepared from different levels from *Nigella Sativa* seeds improved the mean values of serum glucose, as compared to non-treated rats (negative control group). Serum glucose decreased gradually with increasing the levels of *Nigella Sativa* seeds, or increasing the concentration of water extract which prepared from *Nigella Sativa* seeds. The highest decrease in serum glucose recorded for the group which treated with diet containing 10% *Nigella*

Sativa seeds followed by the group treated with water extract prepared from 10% *Nigella Sativa* seeds. These treatments decreased the mean values of serum glucose by about 39.743% and 32.200%, that that of the positive control group, respectively.

Table (4): Effect of Some Levels from *Nigella Sativa* as Seeds or Water Extract on Serum Glucose and Liver Enzymes of Rats Suffering from Hyperlipidemia and Diabetes.

Parameters Groups	Glucose (mg/dl)	U/I	
		AST	ALT
Control (-ve)	88.821 ^g ± 3.893	60.359 ^f ± 5.005	26.884 ^f ± 2.783
Control (+ve)	215.833 ^a ± 5.269	106.450 ^a ± 6.007	61.399 ^a ± 3.653
2.5% <i>N. sativa</i> seed	183.333 ^c ± 2.582	93.487 ^b ± 3.492	54.033 ^b ± 3.495
5% <i>N. sativa</i> seed	169.264 ^c ± 3.687	79.224 ^d ± 3.489	41.116 ^d ± 2.695
10% <i>N. sativa</i> seed	130.054 ± 4.058	70.959 ^e ± 3.220	32.363 ^e ± 2.587
Water extract of <i>N. sativa</i> (2.5%)	192.034 ^b ± 2.768	97.333 ^b ± 3.266	55.779 ^b ± 3.810
Water extract of <i>N. sativa</i> (5%)	178.500 ^d ± 3.209	84.666 ^c ± 3.614	45.500 ^c ± 1.760
Water extract of <i>N. sativa</i> (10%)	146.333 ^f ± 5.465	74.500 ^e ± 2.949	38.333 ^d ± 1.861

LSD: Least significant differences ($P < 0.05$) Mean values in each column with same letters are not significantly different.

In this respect, numerous studies have found increased lipid peroxides or reactive oxygen species (ROS) and oxidative stress or both in different animal models of diabetes (*Friedman et al., 2003*). Oxidative stress refers to an imbalance between the intracellular production of free radicals and the cellular defense mechanism. Protein, lipids, and DNA are sensitive target of ROS. An excess availability of free radicals accompanied by a reduction in the capacity of the natural antioxidant systems leads to cellular dysfunction and death (*Albers and Beal 2000*). Free radical-induced DNA damage has been shown to be increased in embryos from diabetic rats (*Viana et al., 1996*).

There has been increasing interest regarding the role and use of natural antioxidants as a means of preventing oxidative damage in diabetes due to high oxidative stress (*Pritchard et al., 1986*).

The black seed, *Nigella sativa* is known to contain >30% of fixed oil and 0/4-0/45% wt. /wt. of volatile oil. The volatile oil is known to contain 18.4-24% thymoquinone (TQ) and 46% of monoterpenes such as p-cymene and α -piene (*EL-Tahir et al., 1993*).

Ali and Blunden (2003) reported that, the basis of the beneficial effect of *Nigella sativa* in diabetes might be its antioxidant property.

The mean values of serum AST & ALT increased significantly $p < 0.05$ in the positive control group, as compared to the negative control group. Feeding rats on hyperlipidemic diet and treated with alloxan increased serum AST & ALT enzymes by about 76.361% and 128.384%, than that of the negative control group, respectively.

The results in this table indicated that, all treated rats which were suffering from hyperlipidemia and hyperglycemia with *Nigella Sativa* seeds or water extract prepared from different concentrations from *Nigella Sativa* seeds, decreased both AST and ALT enzymes significantly, as compared to the positive control group.

Treating group which suffering from hyperlipidemia and hyperglycemia with hyperlipidemic diet containing 10% *Nigella Sativa* seeds recorded the highest decrease in both AST and ALT enzymes, as compared to other treated groups, followed by the group treated with water extract prepared from 10% *Nigella Sativa* seeds.

In CCl₄-induced toxicity, *Nigella Sativa* oil protected against hepatotoxicity coinciding with improvement in serum lipid profile (*El-Dakhkhny et al., 2000 and Nagi et al., 1999*), decreasing the elevated liver enzyme levels, and increasing the reduced anti-oxidant enzyme levels (*Kanter et al., 2003*). Moreover, treatment with *N. sativa* oil prevented CCl₄-induced liver fibrosis in rabbits with improvement of the anti-oxidant status (*Turkdogan et al., 2001*).

Kanter et al., (2005) reported that, *Nigella sativa* has hepato-protective effect. It protects liver from many toxic metals

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تأثير بعض المستويات من حبة البركة كبذور أو المستخلص المائى على الفئران التي تعاني من ارتفاع مستوى دهون الدم والسكر

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الهدف الرئيسى : من هذه الدراسة هو دراسة تأثير الغذاء المدعم بثلاث مستويات من بذور حبة البركة (٢.٥، ٥، ١٠٪ وزن/وزن) أو المستخلص المائى من بذور حبة البركة (٢.٥، ٥، ١٠٪ وزن/حجم) على جلوكوز الدم ، وصورة الدهون ووظائف الكلى وانزيمات الكبد بالإضافة للتقييم الغذائى للفئران التي تعاني من ارتفاع نسبة الدهون والسكر فى الدم . استخدم إجراء التجربة ٤٨ فأر من ذكور فئران الالبينو وزن ١٣٠ ± ٥ جم قسمت الفئران إلى مجموعتين رئيسيتين . المجموعة الرئيسية الأولى (٦ فئران) تم تغذيتها على غذاء أساسى استخدمت كمجموعة (ضابطة) . أما المجموعة الثانية (٤٢ فأر) تم تغذيتها على غذاء مرتفع الدهون لمدة ٦ أسابيع ، بعد هذه المدة تم حقن فئران المجموعة الثانية بمادة الالوكسان (١٥٠ ملجم /كجم من وزن الجسم) لإحداث مرض السكر . فئران المجموعة الثانية الرئيسية تم تقسيمها عشوائيا إلى ٧ مجموعات فرعية كالتالى : *المجموعة الفرعية الأولى* (١) تم تغذيتها على غذاء مرتفع الدهون استخدمت كمجموعة ضابطة مصابة ، *المجموعات الفرعية الثانية والثالثة والرابعة* تم تغذيتهم على نفس الغذاء والمحتوى على (٢.٥ ، ٥ ، ١٠٪) بذور حبة البركة على التوالي ، *المجموعات الفرعية الخامسة والسادسة والسابعة* تم تغذيتهم غذاء على غذاء مرتفع الدهن ومعالمتهم بالمستخلص المائى من حبة البركة فى ماء الشرب بنسبة (٢.٥ ، ٥ ، ١٠٪ وزن/جم) على التوالي . استمرت فترة التجربة ٢٨ يوما .

أشارت النتائج إلى أن الإصابة بارتفاع مستوى دهون الدم والجلوكوز أدى إلى زيادة معدل الجلوكوز فى الدم ووظائف الكلى وانزيمات الكبد ودهون الدم فيما عدل كولسترول الليبوبروتينات عالية الكثافة HDL.C بالمقارنة بالفئران الأصحاء ، معاملة الفئران التي تعاني من ارتفاع دهون الدم بنسب مختلفة من حبة البركة أو المستخلص المائى أدت إلى تحسين عام لصحة الفئران خاصة عندما استخدم التركيز العالى من البذور أو المستخلص المائى .

ويستخلص من هذه النتائج أن معاملة الفئران التي تعاني من ارتفاع مستوى دهون الدم والجلوكوز ببذور حبة البركة أو المستخلص المائى المعد من بذور حبة البركة ، وخاصة عند استخدام المستويات المرتفعة من البذور أو المستخلص من الممكن استخدامه فى علاج الأشخاص المصابين بارتفاع مستوى دهون الدم والمصابين بالسكر .

الكلمات المفتاحية :

ارتفاع دهون الدم - السكر - فئران - حبة البركة - جلوكوز - صورة الدهون - وظائف الكلى وانزيمات الكبد