

Hypolipidemic and Antioxidant Effects of Fenugreek-Nigella Sativa Combination on Diabetic Patients in Iraq

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ABSTRACT

Background: Dyslipidemia, an established risk factor for coronary heart diseases (CHD), is the most common complication in patients with type 2 diabetes mellitus (T2DM), many hypoglycemic drugs were used in the management of diabetes, because of their cost and many side effects, an alternative herbal therapeutic agent are required, from these plants fenugreek (*Trigonella foenumgraecum* L) and *Nigella sativa* (NS), that found to have hypolipidemic effects in the management of type 2 diabetes mellitus and its serious complications. This study investigates the effect of fenugreek and *Nigella sativa* seeds mixture for controlling hyperglycemia, dyslipidemia and antioxidant effect in type 2 diabetic patients.

Method: A Total of 80 patients (45 males and 35 females) with type 2 DM were recruited in this study, they were divided into two groups: study group (n=40) given 2 g of NS seeds powder and 20 g of fenugreek seeds powder a day for 8 weeks and Control group (n=40), which received the usual treatment protocol, diet, exercise and oral hypoglycemic drugs. The blood sample was collected from each participant before and after study. Investigations include fasting blood glucose, lipid profile test and MDA.

Result: After 2 months of treatment with fenugreek-*Nigella sativa* in the study group, there was a significant difference in the total cholesterol (195.03±8.7 vs. 247.4±9.5), low-density lipoprotein (97.8±7.96 vs. 157.36± 6.8), Triglyceride (192±6.9 vs. 261.8±5.5) as

compared with baseline values. Although the study group showed a significant elevation in HDL, as compared with the control group (p < 0.05) (40.85±6.16 vs. 37.15±3.18), this elevation was not significant as compared to the baseline value (40.85±6.16 vs. 39.93±5.44). MDA in the study group showed significant reduction as compared with its baseline value (1.64±0.8 vs. 2.3±0.5) but this change was nonsignificant as compared with the control group, between groups (1.64±0.8 vs. 1.52±0.30). Fasting blood glucose were not significantly different between the study and control groups.

Conclusion: The combination of fenugreek and *Nigella Sativa* herbs have the most powerful lipid lowering effect in diabetic patients by controlling blood glucose and its effect on dyslipidemia without side effects and also have greater antioxidant activity by reducing the MDA level in diabetic patients, so can be used as an alternative for management of type 2 diabetes.

Keywords: Pharmaceutical compounds; patients; MDA level; *Nigella sativa*

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INTRODUCTION

Diabetes Mellitus is a metabolic disease associated with chronic hyperglycemia, it is still one of the common causes of mortality, and fastest-growing disease worldwide [1,2]. The diabetes mellitus affected 346 million people in the world, according to the World health organization (WHO) report 2011, and its complications caused 3.4 million patients to be died in 2004. This estimated number is expected to be doubled in 2030 [3,4]. The DM. may be due to insulin deficiency that called type 1 diabetes, or due to deficiency of insulin secretion combined with resistance to insulin action, which is called type 2 diabetes, both types can cause serious complications over time such as nephropathy, neuropathy, retinopathy, dyslipidemia and cardiovascular diseases. Type 2 diabetes is more frequent, which represents 90-95 % of cases.

In the Dyslipidemia, type 2 diabetes is common, which characterized by hypercholesterolemia, hypertriglyceridemia, increased level of low density lipoprotein cholesterol (LDLc) and decrease levels of high density lipoprotein cholesterol (HDLc) In spite that the oral hypoglycemic drugs and insulin can control the complications appears early in diabetes, the late serious complications appear in many patients. Many side effects may usually accompanied the uses of these hypoglycemic drugs such as lactic acidosis, abdominal discomfort, severe hypoglycemia and peripheral edema. Therefore the studies should be continued for more effective and lesser side effects new antidiabetic drugs. Herbs and plants are new therapeutic agents that found to have hypolipidemic effects

in the treatment of type 2 diabetes and its complications From these plants fenugreek (*Trigonella foenumgraecum* L) and *Nigella sativa* (NS), several studies revealed that each one of these plants is effective in decrease plasma glucose and serum lipids in diabetes, and if they used in combination they may be more effective in improving the metabolic index [5]. The active components of *Nigella sativa* seeds having the great pharmacological properties, including, antidiabetic, antioxidant, anti-inflammatory, analgesic, antipyretic, antihypertensive, antiasthmatic, antimicrobial, antineoplastic [6]. The holistic medicinal property of *Nigella sativa* seed is due to its major bioactive component thymoquinone. Oxidative stress is lead to oxidative damage of cell which can measure by antioxidant status. Consequently, the natural antioxidants role and use in preventing oxidative stress occur in diabetes have great importance [7]. One of reactive electrophile species is Malondialdehyde (MDA), which is an aldehyde that form a covalent protein and cause toxic stress in cells. This aldehyde production represents a biomarker to evaluate the oxidative stress level in an organism [8].

The results of the effect of the fenugreek and *Nigella sativa* seeds mixture on hyperglycemia and dyslipidemia on type 2 diabetes were evaluated. The effect of the mixture was studied at MDA level.

MATERIALS AND METHODS

Study design

The study was conducted on 80 patients (45 males and 35 females) with type 2 DM. Patients in this study were

recruited from the outpatient clinic in Basra city-southern Iraq, in the period between September 2019 and November 2019. All the patients were informed about the possible effect of the research, and the written informed consent was taken to each patient. The current study was approved by the ethics committee in the college of pharmacy.

Inclusion criteria

The patient included aged 40-60 years old and diagnosed with DM according to the American diabetes association [9].

Exclusion criteria

Patients were excluded if they have a secondary cause of dyslipidemia, ischemic heart disease, liver disease, renal impairment and patients with any diabetic complication. Pregnant and lactating women were also excluded.

Study groups

This is a prospective study, which was conducted to study the hypolipidemic effects of fenugreek and Nigella sativa seeds combination. Only 80 patients fulfilling the requirements of the study, were divided into two groups (study group and control group) through simple random sampling.

Study group (n=40) patients were given 2 g of NS seeds powder and 20 g of fenugreek seeds powder a day for 8 weeks. Control group patients (n=40) were given the usual treatment protocol, which is diet, exercise and oral hypoglycemic drugs.

There was no significant difference in the average ages and sex ratio between the two groups. The history was taken to

all patients in the two groups, and they subject to physical examination and laboratory investigations at the baseline before starting the treatment and after two months. Investigations include fasting blood glucose and lipid profile test. Height, weight, and body mass index were recorded to all patients before and after two months of the study.

Collect test samples

Blood samples were collected after overnight fasting from both study and control groups, into plain tubes and leave to clot. After that centrifuged at 3000 RPM for 10 min and separated the serum. The serum then frozen at -20°C, then used for determination of TC, TG, and HDLc. LDLc was calculated using the Friedwald formula.

STATISTICAL ANALYSIS OF THE RESULTS

The results of experimental tests were analyzed using the statistical system (spss) version 19. The values of the mean standard deviation (SD) and the values of the T test were calculated and compared with the typical values in the global tables. The statistical values have been illustrated using Microsoft Excel (2007) and it has been found that the observed P values are equal to <0.05.

THE RESULTS OBTAINED

A total of 80 patients with type 2 DM were enrolled in this study, they were divided into two groups, group1 represents the control group and group 2 was a study group. The demographic data for the study population have been shown in Table 1. The mean age was 52.6 ± 4.3 and 50.2 ± 4.1 years for the control group and study group respectively.

Table 1: demographic data of the study participants.

	Control group	Study group	P-value
Age(years)	52.6 ± 4.3	50.2 ± 4.1	0.075
Male:female ratio	21:19	24:16	0.682
Body mass index(kg/m ²)	33.13 ± 5.40	32.09 ± 5.4	0.396
Fasting blood glucose (mg/dl)	121.73 ± 1.93	121.0 ± 5.7	0.449

Data expressed as mean±SD; Age, male: female ratio, BMI and fasting blood glucose were not significantly different between the study and control groups. Table 2 represents the change in lipid profile and MDA between the two groups.

Table 2: Comparison of blood lipid profile and MDA level in both study groups; before and after treatment.

parameter	Control group N=40		Study group N=40		P-value
	Baseline	After treatment	Baseline	After treatment	
TC (mg/dl)	210.28±6.73	200.45±5.71*	247.4±9.5	195.03±8.7*	0.001
LDL (mg/dl)	144.95± 4.8	140.37±6.4	157.36± 6.8	97.8±7.96*	0.000
TG (mg/dl)	239.75±11.29	231.18±10.8	261.8±5.5	192±6.9*	0.004
HDL (mg/dl)	37.18±9.14	37.15±3.18	39.93±5.44	40.85±6.16	0.001

MDA (nmol/ml)	1.47±0.30	1.52±0.30	2.3±0.5	1.64±0.8*	0.4
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P value < 0.05 considered as significant values, *significant (p < 0.05) as compared to its baseline values. The Value is expressed as mean ± standard deviation.

Effect on Total Cholesterol (TC)

The study group administered combination of fenugreek and Nigella Sativa seeds powder for two months, the results demonstrate a significant reduction in the serum total cholesterol level as compared with its baseline value (195.03±8.7) after treatment vs. (247.4±9.5) to baseline. Also, it was significantly lower than the total cholesterol level of the control group, (195.03±8.7 vs. 200.45±5.71) after 2 months. The control group had a significant difference as compared with its baseline level (210.28±6.73 vs. 200.45±5.71) as in table 2.

Effect on Low-density lipoprotein cholesterol (LDL)

The low-density lipoprotein reduced significantly (p < 0.05) in the study group after using the combination of fenugreek and Nigella Sativa seeds powder for 2 months as compared with its baseline value (97.8±7.96 vs. 157.36± 6.8) and compared to the control group also show a significant difference (97.8±7.96 vs. 140.37±6.4) as can be seen in figure1. However, the control group had no significant

difference as compared with its baseline serum level (140.37±6.4 vs. 144.95± 4.8).

Effect on Triglyceride

The level of triglyceride in the study group dropped significantly after 2 months of treatment compared with baseline level (192±6.9 vs. 261.8±5.5) and compared with the observe group TG level, through groups (192±6.9 contra 231.18±10.8). However the control group TG level had no significant difference after 60 days as compared with its baseline value (231.18±10.8 vs. 239.75±11.29).

Effect on HDL cholesterol

Serum HDL elevated significantly in the study group, after using treatment combination for 2 months as compared with the control group (p < 0.05) (40.85±6.16 vs. 37.15±3.18) but this elevation was not significant as compared to the baseline value (40.85±6.16 vs. 39.93±5.44). The control group had no significant difference as compared with its baseline level.

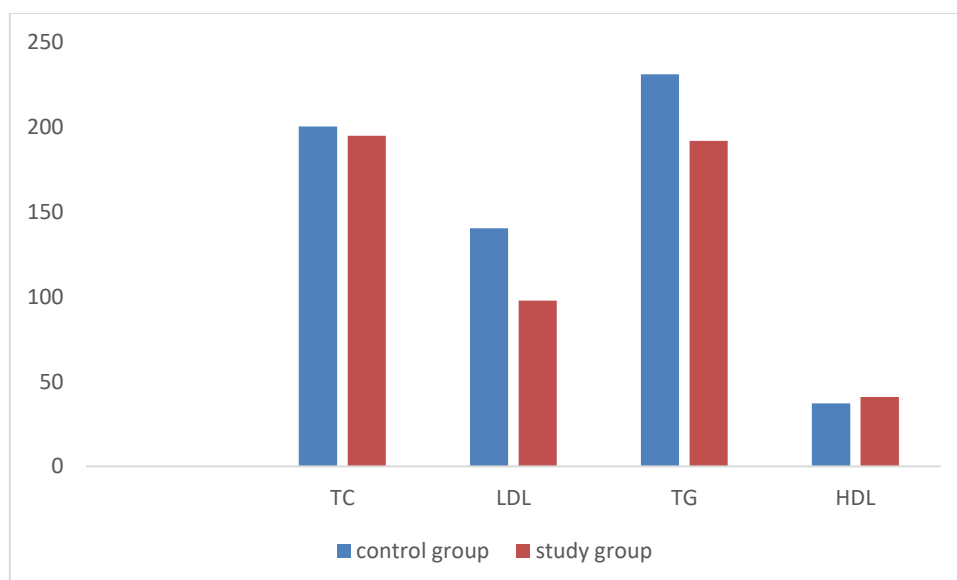


Figure 1: Bar diagram showing the effect of fenugreek-Nigella Sativa seeds combination on lipid profiles.

Effect on MDA

Plasma level of MDA in the study group showed significant reduction after 2 months of treatment as compared with its baseline value (1.64±0.8 vs. 2.3±0.5) but this change was nonsignificant as compared with the control group, between groups (1.64±0.8 vs. 1.52±0.30).

The debate of results

Diabetes mellitus has associated with a high prevalence, morbidity and mortality worldwide. Dyslipidemia affecting almost 50% of patients with T2DM. An increase in the concentration of TC and LDL, and a decrease in HDL are

associated with a raised risk of CHD. This study was conducted to evaluate the effects of herbal compounds contain fenugreek and Nigella sativa seeds combination for controlling hyperglycemia, dyslipidemia and antioxidant effect in type 2 diabetic patients, as an alternative to the pharmacological drugs that used in the management of type 2 DM which may cause many side effects and they used with limitations. Usually, The level of TC, LDL, and TG are elevated in DM as a result of the decrease in insulin secretion and impairment of metabolic process as lipolysis and lipogenesis [10,11]. A lot of studies confirmed the effect of medicinal herbals (Nigella Sativa and fenugreek) that can be increased insulin level and activate with increase the

number of pancreatic β -cell, these studies found a significant reduction in blood glucose level and biochemical enzymes by oral administration of these plants (Sheik, 2019) [12-14].

Fenugreek can increase the glycolysis processes in muscle by progressing the activity of their enzymes, so it has little effect on gluconeogenesis by deactivation of enzymes. It also exerts the hypoglycemic effect via stimulating the synthesis of insulin from pancreatic cells and increases tissue sensitivity. On the other hand, Heshmati et al; 2015, Mohamed et al; 2015, Hamdan et al; 2019 confirmed the effect of Nigella sativa seeds on controlling hyperglycemia when it is combined with oral hypoglycemic drugs by improvement the activity of β -cells and insulin resistance [15-16].

In the current study, the reduction in the fasting blood glucose and weight was not statistically significant, this result was in agreement with (Shafiee-nick et al; 2012) who revealed that the administration of this herbal compound can only inhibit progression and deterioration of hyperglycemia.

In our study, the study group receiving the combination of (Fenugreek seeds and Nigella sativa) for two months shows a significant improvement in dyslipidemia. A significant reduction in TC, LDL, and triglyceride as compared with their baseline lipid profile value and as compared with the control group. Although HDL level was elevated in group using fenugreek and Nigella sativa, but unfortunately, this change was not significant as compared with its baseline, but there was a significant difference when compared with control group. The lowering effect by using herbal combination may be attributed to their stimulation to carbohydrate metabolism, including glucose uptake by the cell, enhance gluconeogenesis, and increase the absorption rate from the gastrointestinal tract and increase insulin secretion [22]. This finding was similar to that conducted by (Mohamed et al. 2015, and Geberemeskel et al, 2019). This result was also in agreement with the results of previous studies, that demonstrated significant reduction in TC, LDL and triglyceride by using Nigella sativa [17]. In contrast, these results were different from that reported by Kassaian et al and Gaddam et al who found no significant effect of fenugreek seeds on lipid profile between study and control groups [18,19], And Qidwai et al 2009 who conducted nonsignificant impact on serum lipid after using Nigella sativa [20-23].

In diabetic treatment, one of the potential strategies is antioxidants, since antioxidant activities have been related to health recommended. Substances like fenugreek and Nigella are rich in antioxidants that can protect the body systems. Fenugreek seed contain high quantity of phenolic and flavonoid constituents that associated with antioxidant properties [24,25]. In addition to that, Nigella sativa contains Thymoquinone which is a scavenger to the free radicals that give it the antioxidant effect [26-28]. MDA is elevated in the diabetic patient as a good marker for lipid peroxidation but it is significantly decreased in the study group after taking the herbals mixture with anti-oxidants effect as compared with its baseline value. This finding was in agreement with (Hamadi et al; 2012 and Salih et al; 2014),

who found that fenugreek reduced MDA. And in line with (Desai et al; 2015 and Akash et al; 2011) that conducted Nigella Sativa inhibit lipid peroxidation that reduced MDA [29-31].

CONCLUSION

The combination of fenugreek and Nigella Sativa herbs have the most powerful lipid lowering effect in diabetic patients by controlling blood glucose and its effect on dyslipidemia without side effects, and greater antioxidant activity by reducing the MDA level in diabetic patients. More studies are required for these plants with different doses and for more indications.

CONFLICT OF INTEREST

There is no conflict of interest to be declared and the study was funded by the researcher themselves.

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