Journal of Medicinal Plants Studies
www.PlantsJournal.com

ISSN (E): 2320-3862
ISSN (P): 2394-0530
www.plantsjournal.com
NAAS Rating: 3.53
JMPS 2020; 8(1): 52-57

Received: 29-11-2019
Accepted: 31-12-2019

Amira E Elfouly
Department of Family Medicine, Faculty of Medicine, Suez Canal University, Egypt

Mosleh A Ismail
Department of Family Medicine, Faculty of Medicine, Suez Canal University, Egypt

Hanan M Kamal
Department of Cardiology, Faculty of Medicine, Suez Canal University, Egypt

Safwat A Ahmed
Department of Pharmacognosy, Faculty of Pharmacy, Suez Canal University, Egypt

Lamiaa E Fiala
[a] Department of Community Medicine, Faculty of Medicine, Suez Canal University, Egypt
[b] Department of Health Sciences, Faculty of Health & Rehabilitation Sciences, Princess Noura Bint Abdulrahman University, Riyadh, Saudi Arabia

Corresponding Author:
Amira E Elfouly
Department of Family Medicine, Faculty of Medicine, Suez Canal University, Egypt

Safety of an intervention with nigella sativa on adult patients with dyslipidemia attending family practice clinic-suez canal university hospital, Ismailia, Egypt

Amira E Elfouly, Mosleh A Ismail, Hanan M Kamal, Safwat A Ahmed and Lamiaa E Fiala

Abstract
Background: Dyslipidemia is responsible for the development of atherosclerotic cardiovascular diseases as ischemic heart diseases. Although statins is the mainstay therapy for dyslipidemia, it has many side effects such as muscle weakness, aching pain, tenderness, cramps. *Nigella sativa* is a herb with many pharmaceutical potential. A lot of animal studies have already been done to determine the various activities of *N. sativa* oil on different components of the metabolic syndrome.
Objectives: Determine safety of *Nigella Sativa* on clinical and biochemical parameters among patients with dyslipidemia.
Subjects and Methods: The study is double blinded trial that was conducted in Family practice clinic, 19 patients were included in intervention group and 19 in control. Intervention group received their routine therapy for dyslipidemia (statins) in addition to crushed nigella sativa seeds daily for 6 weeks. Control group received their routine in addition to placebo. The baseline blood pressure, fasting blood sugar, liver transaminases and serum creatinine were measured before the trial and repeated after 6 weeks.
Results: The patients in the intervention group had significantly lower creatinine level (p=0.037) after intervention. B.P. fasting blood sugar, liver transaminases and serum creatinine measures between both intervention and control groups were not statistically significant after adding nigella sativa. Favorable impact of N. sativa was noted on almost all measures in intervention group but were not statistically significant when compared to control group.
Conclusion: Adding N. sativa to therapy for dyslipidemia is safe on B.P., blood sugar, liver and kidney function tests.

Keywords: Dyslipidemia, *N. sativa*, statins

1. Introduction
Dyslipidemia is responsible for the development of atherosclerotic vascular diseases, such as hypertension, ischemic heart disease, and cerebral stroke [1]. Dyslipidemia is a broad term that refers to a number of lipid disorders. Most (80%) lipid disorders are related to diet and lifestyle, although familial disorders (20%) are important as well. The basic categories of dyslipidemias include: elevated low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), excess lipoprotein (a), hypertriglyceridemia, atherogenic dyslipidemia, and mixed lipid disorders. Most patients with CHD have mixed dyslipidemia [2].
Cardiovascular diseases is now emerging as a major health concern in developing countries, including countries of the Eastern Mediterranean region leading to morbidity and mortality in many countries [3]. Recent evidence suggests that lipid-lowering therapy reduces cardiovascular morbidity and mortality and causes regression of coronary atherosclerosis [4]. Serial studies using Intravascular Ultrasound (IVUS) showed that regression of coronary atherosclerosis induced by intensive statin therapy is related to the large reduction in low-density lipoprotein cholesterol [5].
Alternative medicine has opened new door for the treatment of cardiometabolic disorders which has attained epidemic proportion throughout the world. *Nigella sativa* belonging to the buttercup family Ranunculaceae, is commonly known as black seeds. In South Asia, it is called Kalonji, its Arabic name is Habat-ul-Sauda and its English name is Black cumin. In the Unani Tibb system of medicine, black cumin is regarded as a valuable remedy for a number of diseases.

Sayings of the Islamic prophet Muhammad underline the significance of black cumin. According to a hadith narrated by Abu Hurairah, he says, "I have heard the Messenger of Allah, saying that the black granules (kalonji) is the remedy for all diseases except death [6].

They have been traditionally used in the treatment of a number of ailments including respiratory health, stomach, intestinal health, kidney, hypertension, bladder, liver function, circulatory, immune system support and for general overall wellbeing [7-10]. Numerous traditional applications of *Nigella sativa* seed recorded as medicinal and pharmacological activities [11, 12].

Dyslipidemia is a common risk factor for cardiovascular disease, the leading cause for morbidity and mortality among patients. *Nigella sativa* is an easily available and acceptable remedy to treat dyslipidemia and at a low cost so, there is an immense need to conduct the current study aiming to improve the quality of life of dyslipidemic patients by improving the management strategy of dyslipidemia.

2. Materials and Methods

2.1 Study Setting and Subjects

We conducted a randomized clinical trial at the family practice clinic in Suez Canal University (SCU) Hospital, Ismailia, Egypt. This trial was conducted from February 2018 till August 2018, after being approved by the Medical Ethical Committee at Faculty of Medicine, Suez Canal University. In addition, an informed consent was obtained from each patient. The participants were aged between 40 and 75 years old diagnosed with dyslipidemia and presented to the clinic at SCU Hospital. The patients were included according to the 2013 guidelines of AAC/AHA guidelines [13].

Inclusion criteria for participants

- Individuals with clinical Atherosclerotic Cardiovascular Diseases (ASCVD).
- Individuals with primary elevations of LDL-C >190 mg/dL.
- Diabetics aged 40 to 75 years with LDL-C 70 to189 mg/dL.
- without clinical ASCVD
- Individuals without clinical ASCVD or diabetes with LDL-C 70 to189 mg/dL and estimated 10-year ASCVD risk >7.5%

Exclusion criteria for participants

- Patients with mental disorders that interfere with the adherence to the recommended interventions.
- Pregnant and lactating women.
- Decompensated liver diseases (elevated AST, elevated ALT).
- Chronic kidney diseases (Glomerular filtration rate <30 mL/min
- Elevated S. Creatinine or elevated BUN).
- Known malignancies.
- Patients previously taking statin therapy.

2.2 Study procedure

We enrolled fourty patients in this trial. Patients were randomly allocated to two groups; the interventional and control groups, each group consisted of 20 patients. Data describing the socioeconomic status, education, occupation, and income were obtained from the participants. Then, all patients were subjected to full medical history taking and clinical examination. Patients in the interventional group received crushed *Nigella sativa* seed extracts, 1g capsule once daily, for 6 weeks and the anti-dyslipidemic drug (Atorvastatin) while Control comparator received Placebo which is dietary supplement (starch powder) 1g capsule once daily, for 6 weeks and the anti-dyslipidemic drug (Atorvastatin).

2.3 Outcome measures

The outcome measures for the trial were fasting blood sugar, liver transaminases and serum creatinine measured after six weeks of intervention. Also the anthropometric measurements were assessed before and after 6 weeks of intervention with nigella sativa.

2.4 Statistical Analysis

Statistical analysis had been performed using SPSS version 23 for windows software XP version. Data was presented using descriptive statistics in the form of frequencies and percentages for qualitative variables, means and standard deviations for quantitative variables. Independent student t test & Mann-Whitney U tests were used for comparison of continuous variables between study groups, and paired-sample student t test & Wilcoxon Signed Ranks Test were used for within-group analyses of change. The Chi-square (X^2 test) had been used to compare frequency ratios between groups. Whenever the expected values in one or more of the cells in a 2x2 tables was less than 5, Fisher exact test was used instead. Pearson's correlation coefficient was used to determine associations between different variables. P value of less than 0.05 had been considered statistically significant.

3. Results

Table 1 shows socio-demographic characteristics of patients in both groups. Age in both groups was comparable, with mean age 50.84±7.52 years in intervention group and 56.26±9.52 years in control group, females represented 89.5% of the intervention group, meanwhile females formed 94.7% of the control group. There was no significant difference between the two groups in the gender distribution (p=0.54). Also about 68.4% of patients in intervention group live in rural area as the same 68.4% of patients in control group live in urban area. Finally, there was no significant difference between the two groups in any of these characteristics except that higher family members significantly more prevalent in control group.

Table (2) shows socioeconomic characteristics of patients in both groups. The most frequent patient education level in intervention and control groups was illiteracy or being able to read and write only (63.2%) and (89.5%), respectively. Likewise, the most frequent spouse education level in intervention and control groups was illiteracy or being able to read and write only (47.4 %) and (78.9%), respectively. Most patients were unemployed (housewives) (86.8%) while most of spouses are unskilled manual worker, skilled manual worker or works in trades (68.4%).

Table (3) summarizes the medical history of patients in both groups. 78.9% of the patients are found to have diabetes and hypertension while 18.4% have diabetes only.

Table (4) shows clinical assessment of patients in both groups before intervention with nigella sativa and there was no statistically significant difference between the intervention group and control group in any of these clinical parameters (p>0.05).

Table (5) shows clinical assessment of patients in both groups after intervention with nigella sativa and there was no

statistically significant difference between the intervention group and control group in any of these clinical parameters (p>0.05).

Table (6) shows Comparison between both groups regarding laboratory measures before intervention with nigella sativa. There was no statistically significant difference between the intervention group and control group in any of these laboratory measures (p>0.05).

Table 10 shows Comparison of reported side effects of patients in both groups shows that patients in the study group had significantly lower headache incidence compared to that in control group (p=0.005).

Table 1: Socio-demographic characteristics (SDC) in both groups part 1 (N=38)

SDC	Interventional group (N=19) (NO=%)	Control group (N=19) (NO=%)	Total (N=38) (N0=%)	test value	p-value
Age (years) mean ± SD	50.84±7.52	56.26 ± 9.52	53.55 ± 8.89	1.947	0.059[a]
Gender					
▪ Male	2 (10.5)	1 (5.3)	3 (7.9)	0.36	0.54 [b]
▪ Female	17 (89.5)	18 (94.7)	35 (92.1)		
Residency					
▪ Rural	13 (68.4)	6 (31.6)	19 (50)	5.16	0.023[c]
▪ Urban	6 (31.6)	13 (68.4)	19 (50)		
Number of family member					
▪ < 5 members	14 (73.7)	5 (26.3)	19 (50)	8.53	0.004[c]
▪ ≥ 5 members	5 (26.3)	14 (73.7)	19 (50)		
Usual source of health care					
▪ Covered by health insurance	17 (89.5)	18 (94.7)	35 (92.1)	0.362	0.9[b]
▪ Uncovered by health insurance	2 (10.5)	1 (5.3)	3 (7.9)		

[a] values are based on independent student t-test. Statistical significance at P<0.05

[b] values are based on Fisher's Exact test. Statistical significance at P<0.05

[c] values are based on Chi-square test. Statistical significance at P<0.05

Table 2: Socio-demographic characteristics in both groups part 2 (N=38)

SDC	Intervention group (N=19) (NO=%)	Control group (N=19) (NO=%)	Total (N=38) (NO=%)	test value	p-value
Patient education					
▪ Illiterate or read and write	12 (63.2)	17 (89.5)	29 (76.3)	3.686	0.151[a]
▪ Primary or Preparatory	2 (10.5)	0	2 (5.3)		
▪ Secondary or intermediate or university	5 (26.3)	2 (10.2)	7 (18.4)		
Spouse education					
▪ Illiterate or read and write	9 (47.4)	15 (78.9)	24 (63.2)	3.93	0.195 [a]
▪ Primary or Preparatory	3 (15.8)	1 (5.3)	4 (10.5)		
▪ Secondary or intermediate or university	7 (36.8)	3 (15.8)	10 (26.3)		
Patient occupation					
▪ Unemployed	15 (78.9)	18 (94.7)	33 (86.8)	3.117	0.23 [a]
▪ Unskilled manual worker, Skilled manual worker or trades	3 (15.8)	0	3 (7.9)		
▪ Professional	1 (5.3)	1 (5.3)	2 (5.3)		
Spouse occupation					
▪ Unemployed	2(10.5)	0	2 (5.3)	2.048	0.484 [a]
▪ Unskilled manual worker, skilled manual worker or trades	13(68.4)	13 (68.4)	26 (68.4)		
▪ Professional	4(21.1)	6 (31.6)	10 (26.3)		
Items owned by the family (Family possessions), mean± SD	7.53±2.04	7.74±1.85	5.18±1.16	145.5	0.311 [b]
Crowding index					
≤ 1 person per room	16 (84.2)	9 (47.7)	25 (65.8)	5.73	0.017 [c]
> 1 person per room	3 (15.8)	10 (52.6)	13 (34.2)		
Total SES[d] Score, mean ±SD	32.21 ± 12.25	27.78 ± 10.02	30 ± 11.26	149.5	0.37 [b]

[a] values are based on Fisher's Exact test. Statistical significance at P<0.05

[b] values are based on independent student t-test. Statistical significance at P<0.05

[c] values are based on chi-square test. Statistical significance at P<0.05

[d] socioeconomic status

Table 3: Comparison between intervention & control groups regarding their comorbid diseases (N=38)

Variables	Intervention group (N=19) (NO=%)	Control group (N=19) (NO=%)	Total (N=38) (NO=%)
Chronic illnesses	19 (100)	19 (100)	38 (100)
Hypertension only	1 (2.6)	0	1 (2.6)
Diabetes only	4 (21.1)	3 (15.8)	7 (18.4)
Diabetes + hypertension	14 (73.7)	16 (84.2)	30 (78.9)

Table 4: Comparison between intervention & control groups regarding pre-intervention clinical assessment (N=38)

Variables	Intervention (N=19) mean ± SD	Control (N=19) mean ± SD	Total (N=38) mean ± SD	test value	p-value
Baseline anthropometric measurements					
Weight (kg)	88.74±13.03	93.16±19.88	90.95±16.73	0.811	0.432 [a]
Height (cm)	157 (154-160)	160 (154-163)	158 (154-160)	149.5	0.37 [b]
BMI (kg/m^2)	35.83±5.28	37.04±7.81	36.44±6.60	0.559	0.58 [a]
Waist circumference (cm)	113.47±10.11	114.79±11.66	114.13±10.78	0.372	0.712 [a]
Hip circumference (cm)	121.42±11.66	122.89±13.84	122.16±12.65	0.355	0.725 [a]
Waist/hip ratio	0.94±0.04	0.94±0.04	0.94±0.04	0.034	0.973 [a]
Baseline blood pressure					
Systolic (mm/Hg)	130 (120-160)	120 (120-140)	130 (120-140)	132	0.163 [b]
Diastolic (mm/Hg)	80 (70-90)	70 (80-90)	80 (70-90)	120	0.08 [b]

[a] values are based on Independent t-test. Statistical significance at $P<0.05$

[b] values are based on Mann-Whitney U test. Statistical significance at $P<0.05$

Parametric data were presented as mean ± standard deviation (SD), while non-parametric data were presented as median (25th - 75th percentile)

Table 5: Comparison between intervention & control groups regarding post-intervention clinical assessment (N=38)

Variables	Intervention (N=19) mean ± SD	Control (N=19) mean ± SD	Total (N=38) mean ± SD	test value	p-value
Post-intervention anthropometric measurements					
Weight (kg)	88.05±12.42	94.42±20.84	91.24±17.22	1.144	0.26 [a]
BMI (kg/m^2)	35.56±5.10	37.51±8.05	36.54±6.72	0.891	0.379 [a]
Waist circumference (cm)	114 (104-118)	116 (109-118)	116 (105-118)	165	0.665 [b]
Hip circumference (cm)	119.53±10.99	123.79±14.81	121.66±13.04	0.344	0.733 [a]
Waist/hip ratio	0.94±0.04	0.94±0.05	0.94±0.04	-0.172	0.865 [a]
Post-intervention blood pressure					
Systolic (mm/Hg)	120 (120-140)	110 (13-150)	125 (120-140)	173	0.84 [b]
Diastolic (mm/Hg)	80 (80-90)	80 (70-90)	80 (80-90)	154	0.452 [b]

[a] values are based on Independent student t-test. Statistical significance at $P<0.05$

[b] values are based on Mann-Whitney U test. Statistical significance at $P<0.05$

Parametric data were presented as mean ± standard deviation (SD), while non-parametric data were presented as median (25th - 75th percentile)

Table 6: Comparison between intervention & control groups regarding pre-intervention laboratory measures (N=38)

Pre-intervention Laboratory measures	Interventional group (N=19) mean ± SD	Control group (N=19) mean ± SD	Total (N=38) mean ± SD	Test value	p-value
FBS (mg/dl)	160(140-230)	210 (139-251)	181.5 (139-248)	136	0.201 [b]
Creatinine (mg/dl)	0.6 (0.6-0.8)	0.7 (0.6-0.8)	0.6 (0.6-0.8)	137.5	0.212 [b]
ALT (IU/dl)	25.53±10.42	22.47±9.92	24.00±10.15	-0.925	0.361 [a]
AST (IU/dl)	20 (17-23)	18 (13-26)	19 (14-23)	157.5	0.51 [b]

[a] values are based on Independent t-test. Statistical significance at $P<0.05$

[b] values are based on Mann-Whitney U test. Statistical significance at $P<0.05$

Parametric data were presented as mean ± standard deviation (SD), while non-parametric data were presented as median (25th - 75th percentile)

Table 7: Comparison between intervention & control groups regarding post-intervention laboratory measures (N=38)

Post-intervention Laboratory measures	Intervention group (N=19) mean ± SD	Control group (N=19) mean ± SD	Total (N=38) mean ± SD	Test value	p-value
FBS (mg/dl)	142 (120-223)	210 (139-251)	162.5 (123.5-248.7)	130	0.146[b]
Creatinine (mg/dl)	0.66±0.15	0.74±0.14	0.71±0.14	109.5	0.037[a]
ALT (IU/dl)	18 (16-34)	20 (15-28)	18.5 (15.7-30.2)	164.5	0.644[b]
AST IU/dl)	18 (16-21)	18 (13-26)	18 (14.75-22)	157	0.506[b]

[a] values are based on Independent t-test. Statistical significance at $P<0.05$

[b] values are based on Mann-Whitney U test. Statistical significance at $P<0.05$

Parametric data were presented as mean ± standard deviation (SD), while non-parametric data were presented as median (25th - 75th percentile)

Table 8: Laboratory measures in the intervention group pre and post intervention (N=38)

Laboratory measures	Pre-intervention (N=19) mean ± SD	Post-intervention (N=19) mean ± SD	test value	p-value
FBS (mg/dl)	160 (140-230)	142 (120-223)	-0.382	0.702 [a]
Creatinine (mg/dl)	0.6 (0.6-0.8)	0.6 (0.6-0.7)	-1.05	0.293 [a]
ALT (IU/dl)	26 (20-30)	18 (16-34)	-0.611	0.541 [a]
AST IU/dl)	20 (17-23)	18 (16-21)	-0.04	0.968 [a]

[a] values are based on Wilcoxon Signed Ranks Test. Statistical significance at $P<0.05$

[b] values are based on Paired t-test. Statistical significance at $P<0.05$

Parametric data were presented as mean ± standard deviation (SD), while non-parametric data were presented as median (25th - 75th percentile)

Table 9: Laboratory measures in the control group pre and post intervention (N=38)

Laboratory measures	Pre-intervention (N=19) mean ± SD	Post-intervention (N=19) mean ± SD	test value	p-value
FBS (mg/dl)	210 (139-251)	189 (124-295)	-0.218	0.828 [a]
Creatinine (mg/dl)	0.7 (0.6-0.8)	0.7 (0.6-0.8)	-0.516	0.606 [a]
ALT (IU/dl)	22 (15-28)	20 (15-28)	-0.698	0.485 [a]
AST IU/dl)	18 (13-26)	19 (14-25)	-0.547	0.584 [a]

[a] values are based on Wilcoxon Signed Ranks Test. Statistical significance at $P<0.05$

[b] values are based on Paired t-test. Statistical significance at $P<0.05$

Parametric data were presented as mean ± SD, while non-parametric data were presented as median (25^{th} - 75^{th} percentile)

Table 10: Comparison of reported side effects of patients in both groups (n=38)

Variables	Total (n=38) N (%)	Intervention group (n=19) N (%)	Control group (n=19) N (%)	test value	p-value
Baseline side effects					
Fatigue	19 (50)	8 (42.1)	11 (57.9)	0.947	0.533 [a]
Muscle pain	10 (26.3)	3 (15.8)	7 (36.8)	2.17	0.141 [a]
Headache	12 (31.6)	4 (21.1)	8 (42.1)	1.94	0.163 [a]
Abdominal pain	3 (7.9)	0	3 (15.8)	3.25	0.23 [b]
Diarrhea	4 (10.5)	2 (10.5)	2 (10.5)	0.001	0.9 [b]
Constipation	7 (18.4)	2 (10.5)	5 (26.3)	1.62	0.41 [b]
Post-intervention					
Fatigue	15 (39.5)	6 (31.6)	9 (47.4)	0.991	0.319 [a]
Muscle pain	7 (18.4)	2 (10.5)	5 (26.3)	1.62	0.41 [b]
Headache	12 (31.6)	2 (10.5)	10 (52.6)	7.79	0.005 [a]
Abdominal pain	4 (10.5)	2 (10.5)	2 (10.5)	0.001	0.9 [b]
Diarrhea	3 (7.9)	2 (10.5)	1 (5.3)	0.362	0.9 [b]
Constipation	6 (15.8)	1 (5.3)	5 (26.3)	3.16	0.18 [b]

[a] values are based on Chi-square test. Statistical significance at $P<0.05$

[b] values are based on Fisher's Exact test. Statistical significance at $P<0.05$

4. Discussion

This trial evaluated the outcome and safety of crushed nigella sativa seeds in dyslipidemic patients. Our study revealed that patients in the intervention group had lower levels of serum creatinine after 6 weeks of intervention with 1gm nigella sativa compared to the control group l (p=0.037). Most of the current study patients in both groups were obese, the mean BMI was (35.83±5.28 versus 37.04±7.81 in the intervention and control groups respectively). These were in disagreement with Qidwai *et al*. [14] who showed lower body mass index (BMI; 27.13± 3.88 versus 28.26±6.75 in the intervention and control groups respectively). Also the finding were in disagreement with Amin *et al*. 2015 [15] who showed (BMI; 27.2±3.0 versus 27.3±3.5 in the intervention and control groups respectively).

The majority of the study participants had hypertension with the mean systolic blood pressure was (133.42±20.42 versus 125.26±15.41 in the intervention and control groups respectively). The results were in consistence with Qidwai *et al*. [14] who showed that the mean systolic BP (128.90±18.37 versus 122.30±17.76 in the intervention and control groups respectively).

The mean systolic blood pressure after 6 weeks was 126.84±16.35mmhg for intervention group compared to 128.95±21.05 mm hg for the control while the mean diastolic blood pressure after 6 weeks was 84.74±11.24mmhg for intervention group compared to 82.11±13.57mmhg for control group; the differences were not statistically significant, These results were in disagreement with the study conducted by Dehkordi in 2008 [16] using 200mg nigella sativa oil as an intervention with a mean SBP in intervention group 149.5±1.3 versus 148.2±1.2 in placebo group). This difference may be due to different methodology. We had reported mild side effects after 6 weeks, fatigue was the most prevalent side effect among patients in the intervention group (31.6%), whereas more than half of the patients in the control group suffered from headache (52.6%).

5. Limitations of the current study

The strengths of the present study were its prospective, randomized controlled double blinded design, stable treatment regimen throughout the study and objective assessment of end points, but this study also had some limitations as small sample size compared to other studies' sample size and intervention with nigella sativa as an add on drug to the recommended treatment of dyslipidemic patients (not a separate arm) so the effect of nigella sativa alone was not calculated.

6. Conclusions

The current study concluded that *N. sativa* was safe and effective with less side effects than statins as an add on drug in the management strategy of patients with dyslipidemia and this improve the quality of life for these patients.

7. References

1. Johnson ML, Pietz K, Battleman DS, Beyth RJ. Prevalence of comorbid hypertension and dyslipidemia and associated cardiovascular disease. Heart disease (CHD). 2004; 2:3.
2. Smith G. Epidemiology of dyslipidemia and economic burden on the healthcare system. American journal of managed care. 2007; 13(3):S68.
3. Alwan AA. Cardiovascular diseases in the eastern Mediterranean region. World health statistics quarterly. Rapport trimestriel de statistiques sanitaires mondiales. 1993; 46(2):97-100.
4. Ridker PM, Danielson E, Fonseca FA. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N. Engl. J Med. 2008; 359:2195-207.
5. Okazaki ST. Yokoyama Miyauchi. Early statin treatment in patients with acute coronary syndrome: Demonstration of the beneficial effect onatherosclerotic lesions by serial volumetric intravascular ultrasound analysis during half a year after coronary event: The establish study. Circulation.

2004; 110:1061-1068.
6. Al-Bukhari MI, Sahi AB. The collection of authentic sayings of Prophet Mohammad (peace be upon him), division 71 on medicine. Hilal Yayinlari, Ankara, Turkey, 1976.
7. Başer KH, Honda G, Miki W. Herb drugs and herbalists in Turkey. Institute for the Study of Languages and Cultures of Asia and Africa, 1986.
8. Deliorman D, Çalış İ, Ergun F, Doğan BS, Buharalıoğlu CK, Kanzık I. Studies on the vascular effects of the fractions and phenolic compounds isolated from *Viscum album* ssp. album. Journal of ethnopharmacology. 2000; 72(1-2):323-9.
9. Pieroni A, Price L. Eating and healing: traditional food as medicine. CRC Press, 2006.
10. Malhotra SK, Nigella I, Peter, KV. Hand book of Herbs and Spices, 2006, 2.
11. Gilani AU, Jabeen Q, Khan MA. A review of medicinal uses and pharmacological activities of Nigella sativa. Pak J Biol. Sci. 2004; 7(4):441-51.
12. Ramadan MF. Nutritional value, functional properties and nutraceutical applications of black cumin (*Nigella sativa* L.): an overview. International journal of food science & technology. 2007; 42(10):1208-18.
13. Stone NJ *et al*. ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll. Cardiol. 2013-2014; 63:2889-2934.
14. Qidwai W, Hamza HB, Qureshi R, Gilani A. Effectiveness, Safety, and Tolerability of Powdered Nigella sativa (Kalonji) Seed in Capsules on Serum Lipid Levels, Blood Sugar, Blood Pressure, and Body Weight in Adults: Results of a Randomized, Double-Blind Controlled Trial. J Altern Complement Med. 2009; 15(6):639-44.
15. Amin F, Islam N, Anila N, Gilani AH. Clinical efficacy of the co-administration of Turmeric and Black seeds (Kalongi) in metabolic syndrome-A double blind randomized controlled trial-TAK-Met S trial. Complement Ther Med. 2015; 23(2):165-74.
16. Dehkordi FR, Kamkhah AF. Antihypertensive effect of Nigella sativa seed extract in patients with mild hypertension. Fundam. Clin. Pharmacol. 2008; 22(4):447-52.