REVIEW ARTICLE

Effects of *Nigella sativa* supplementation on blood parameters and anthropometric indices in adults: A systematic review on clinical trials

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Background: *Nigella sativa* (*N. sativa*) has been used in traditional medicine and several studies have been performed in the last decades to reveal the effects of it on different medical disorders such as diabetes, dyslipidemia, hypertension, and obesity. We evaluated the effects of *N. sativa* supplementation on lipid profiles, glycemic control, blood pressure (BP), and some anthropometric indices in humans. **Materials and Methods:** A search on published studies was done by using databases including PubMed, Google Scholar, Thomas Reuters Web of Science, and Cochrane. Medical subject headings (MeSH) terms searched included "*N. sativa*," "Black seed," "Black cumin," "kalonji," and "Triglycerides," "Cholesterol," "Lipoproteins," "LDL," "Lipoproteins," "HDL," "Blood glucose," "Hemoglobin A," "Glycosylated," "Blood pressure", "Body mass index," "Waist circumference". Initially 515 articles were extracted. Four hundred ninety-two papers that were unrelated, reviews, animal studies, and combined and duplicated studies were excluded, 23 articles were eligible for this review. **Results:** After analyzing 23 articles including 1531 participants, these results were achieved: In 4 trials, *N. sativa* reduced BP, but in 5 trials it could not. Fasting blood sugar (FBS) was reduced significantly in 13 studies. In addition, *N. sativa* reduced levels of glycosylated hemoglobin (HbA1c). Although weight and waist circumference (WC) in 2 articles were reduced significantly, in 6 articles they were not. Fluctuation in lipid profile in the articles was very controversial, being significant in many of them but not in others. **Conclusion:** Our systematic review revealed that *N. sativa* supplementation might be effective in glycemic control in humans.

Key words: Anthropometric indice, glycemic control, lipid profile, *Nigella sativa*

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INTRODUCTION

In the beginning of human life, plants were used as medicines.[1] Nowadays there is much more attention paid to the use of plants as therapeutics because of lower adverse effects. *Nigella sativa* (black seed), which belongs to family of Ranunculaceae, has been used to improve health and cure diseases for centuries, especially in the Middle East and Southeast Asia.[2] A great focus has been placed on several traditional uses and therapeutic properties of *N. sativa*.[3]

The pharmacological properties of *N. sativa* is attributed to several component including proteins, amino acids, carbohydrates, fibers, oils (combination of fatty acids, especially polyunsaturated fatty acids), volatile oil (frequently thymoquinone), mineral, alkaloids, flavonoids, saponins, and others.[4]

Effects of *N. sativa* are reported in experimental models, including hypoglycemic,[5] antihyperlipidemic,[6] antihypertensive,[7] antioxidant,[8] and antiinflammatory[9] properties. Several studies showed the different activities of *N. sativa* on the parameters of the metabolic syndrome, such as blood glucose, lipid profile, and blood pressure (BP).[10]

N. sativa is a rich source of unsaturated fatty acids such as linoleic acid and oleic acid and it contains small

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amount of linolenic, arachidonic, and eicosenoic acid, which constitute 80–84% of fatty acids in this seed and may have roles in the hypolipidemic effect of this plant.[11] However, there was no effect of black seed on lipid profiles in some animal studies.[12]

It was also shown that *N. sativa* contains several chemicals (such as thymoquinone) that provide antioxidant activity and diuretic effect, which may play roles in reducing hypertension.[13,14]

However, the cardiovascular properties of *N. sativa* are controversial because some studies show decrease in BP[15,16] but others report no effect in animals[17] or humans.[18]

In the field of blood glucose-lowering effect of *N. sativa*, it has been proposed that activation of insulin secretion[19] and antioxidant action[20] of this seed may be the reason for this effect. However, it was reported to have no effect in some studies.[21]

In some animal studies, it was reported that *N. sativa* has an antiobesity property. The reasons for this effect are not so clear, but factors such as reduction of appetite are proposed.[22]

There are a few review articles[23-25] that have surveyed the effect of *N. sativa* on some diseases. In these research projects, the role of this plant as a treatment factor is evaluated but only a section of parameters was investigated, such as lipid profile in diabetes,[23] BP,[24] or antioxidant activity.[25] Therefore, we are going to review the effect of *N. sativa* supplementation on different clinical and biochemical parameters in humans, the majority of which exist in metabolic syndrome.

MATERIALS AND METHODS

The protocol that was used in this study is the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist. A search of published studies was performed by using computer databases including PubMed, Google Scholar, Thomas Reuters Web of Science, and Cochrane.

Searching was done for articles in the English language until June 2014. Medical subject headings (MeSH) terms included: ("Nigella sativa" [MeSH] OR "blackseed" [tiab] OR "blackcumin" [tiab] OR "Kalonji" [tiab]) AND "Triglycerides" [MeSH] OR "Cholesterol" [Mesh] OR "Lipoproteins, LDL" [MeSH] OR "Lipoproteins, HDL" [MeSH] OR "Blood glucose" [MeSH] OR "Hemoglobin A, Glycosylated" [MeSH] OR "Blood pressure" [MeSH] OR "Body mass index" [MeSH] OR "Waist circumference" [MeSH]).

Primary outcome: Blood glucose
Secondary outcome: Nausea

Inclusion criteria

1. The effect of *N. sativa* on clinical or biochemical parameters.
2. Clinical trial.

Exclusion criteria

1. Animal studies.
2. Review studies.
3. The effect of *N. sativa* on unrelated blood or clinical parameters.
4. The effect of *N. sativa* in combination with other plants or exercise.
5. Duplicated studies.

Data extraction

The following data were extracted: Author, country of study, date of publication, study design, duration of study, aims, number and age of persons, dose of supplement, score of study, and effects of intervention.

Quality of studies

In scoring studies, the trials were stratified based on a scoring checklist as Down Quality Assessment scores.[26] Trials were stratified in this checklist based on acquired scores [Appendix].

Study selection

Initially, 515 articles were extracted. After reviewing their titles and abstracts and removing unrelated, animal, and review studies, 28 articles were retrieved for further evaluation. Finally, 23 studies were considered eligible for our review [Table 1].

The eligible articles were published until June 2014. Five articles could not be included in this review as 3 of them evaluated the effect of *N. sativa* in combination with other plants or exercise. The other 2 were duplicated.

RESULTS

Characteristics of the included studies

All of the studies were clinical trials (of course 5 articles were quasi-experimental). These surveys have been done on different patients and subjects such as 5 studies[27-31] on

Table 1: Process of study selection

Process	Selected studies
Initial search (based on MeSH terms)	515 papers
After exclusion of studies that were unrelated to our study, including effects of *N. sativa* on unrelated parameters and others	76 papers
After exclusion of animal studies	52 papers
After exclusion of review studies	28 papers
After exclusion of combined studies	25 papers
After exclusion of duplicated studies	23 papers

Appendix: Scoring of studies in the systematic review based on Downs Quality Assessment score

Item	Hoseini hf	Dehk-ordi	Hoseini ms	Qidwai	Mohta-shami	Datau	Sabzgh-abaee	Bamosa 2010	Kaatabi	Bilal	Ibrahim rm	Najmi 2012	Najmi 2012	Ibrahim rm	Najmi 2007	Bamosa 1997	Ibrahim da	Shah	Bhatti	Elre-hany	Haque	Najmi 2008	Ahmed
1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
3	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	-
4	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
5	+	+	+	+	-	-	+	-	+	+	+	-	-	+	-	-	-	+	+	-	-	-	-
6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
7	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
8	+	+	+	+	+	+	+	+	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-
9	+	+	+	+	+	+	+	+	+	+	-	-	-	-	-	+	-	-	-	-	-	-	-
10	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
11	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
12	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
13	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
14	+	+	+	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
15	+	+	+	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
16	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
17	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
18	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
19	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
20	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
21	+	+	+	+	+	-	+	+	+	-	+	-	+	-	-	-	+	-	-	-	-	-	-
22	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
23	+	+	+	+	+	+	+	-	-	-	+	+	+	+	+	-	-	-	+	-	-	-	-
24	+	+	+	+	+	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-
25	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
26	+	+	+	+	+	+	+	+	-	+	-	-	-	-	-	+	-	-	-	-	-	-	-
27	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total score	24	24	24	24	23	22	21	19	19	18	18	17	17	17	16	16	16	16	16	15	15	14	14

diabetic patients, 7, trials[32-38] on patients with metabolic syndrome, 4 studies[39-42] on patients with hyperlipidemia, 2 articles[43,44] in the field of hypertension and coronary disease, 1 study[45] on obese men and others were investigated in healthy subjects.[45-48]

With regard to the form of supplement, 2 studies[31,43] have used extract of *N. sativa*, 8 articles[28,30,32,37,38,44,46,48] used oil from the seed, and in the others, that is, 13 articles, powder of *N. sativa* was provided for subjects. The total number of subjects in the trials was 1531. The duration of the trials was between 2 weeks and 6 months. The dose of *N. sativa* supplements was between 200 mg and 5 g per day and was administered orally in all studies. The age range of the participants in trials was 18-65 years old.

With regard to the quality of the research based on Down Quality Assessment scores,[26] 5 studies[30,39,43,46,49] showed double blinding of intervention and 13 trials[30,34-39,41-43,46,48,49] demonstrated appropriate randomization, but in the other studies randomization or blinding was unclear.

The characteristics of 18 included clinical trials are shown in Table 2.

Five articles[27-29,40,47] had no control group and were quasi-experimental studies [Table 3].

In 9 studies,[27,29,30,39,41,43,46-48] there were similar baseline characteristics between groups.

Eight trials[27-29,39,41,43,45,49] reported the rate of dropouts, but in all of them the rate was more than 10%, as in 1 article[28] it was 42%, which naturally affected the results of the study.

In 6 studies,[28,34,35,42,47,49] sample sizes were 10-41 and in the others were 55-161 subjects.

Effects of *N. sativa* on different clinical and biochemical parameters

Effect on lipid profiles

1. Triglyceride (TG)
   The influence of *N. sativa* in lowering TG was effective in 7 trials.[29,31,34,40-42,44]
   This effect in 10 studies was not significant.[30,32,33,35,37,39,43,45,47,49]
2. Total cholesterol (TC)
   In 10 studies *N. sativa* reduced TC significantly.[29,30-32,34,40,41,42,44,45]
   This effect was not found in 4 trials.[33,37,39,47]
3. Low-density lipoprotein (LDL)
   Reduction of LDL was reported significantly in 11 studies.[29,31-35,37,40-42,44]
   This reduction was not significant in 3 articles.[30,39,47]
4. High-density lipoprotein (HDL)
   N. sativa increased HDL in 6 trials.[29,31,33,37,40,44]
   The elevation of this parameter was not significant in 10 studies.[30,32,34,35,39,41-43,47,49]

Effect on glycemic control

1. Fasting blood sugar (FBS)
   FBS was affected by *N. sativa* and reduced notably in 13 studies.[27,28,30-35,37,42,45,47,48]
   In 3 articles this effect was not significant.[39,41,49]
2. Glycosylated hemoglobin (HbA1c)
   This parameter reveals the condition of the blood glucose level from several weeks ago (6-8 weeks) and is a part of the glucose in serum that is combined with hemoglobin. In normal circumstances this parameter should be <6%. In all of the trials that evaluated this factor,[27,30,35,48] *N. sativa* could reduce the level of this factor significantly. This reduction was accompanied by the lowering of the FBS level.

Effect on blood pressure (BP)

One of the most important factors in cardiovascular disease and metabolic syndrome is BP. In 4 studies, *N. sativa* could reduce this factor.[36,43,44,46]

However, this effect was not shown in 5 trials.[33,37,39,42,49]

Effect on some anthropometric parameters

Weight and body mass index (BMI)

These parameters were evaluated in 8 studies. Two trials[30,49] have demonstrated the effect of *N. sativa* in lowering weight and BMI significantly, but in the other articles this effect was not seen.[33,34,37,38,39,43]

Overweight and obesity, especially central obesity, is associated with metabolic disturbances such as diabetes and dyslipidemia.

Waist circumference (WC)

WC plays an important role in the detection of metabolic syndrome. From these studies, 6 trials evaluated this parameter and of them only 1 article[49] showed the reduction of WC, and in 5 articles this was not significant.[32,33,37-39]

In 1 study, lowering of WC was accompanied by the reduction of weight.[49]

Toxicity

Attention to the adverse effect of *N. sativa* supplement is reported in 10 trials.[27,30,35,36,39,41,43,46,48,49]

Only in 2 studies,[30,46] did a few participants who received *N. sativa* oil at the dose of 5 mL per day experience mild nausea,

Table 2: Characteristics of included studies (clinical trials) (listed based on acquired score)

Author	Date of publication	Study design	Duration of study	Aims	*N* (case/control)	Age of subject (years)	Dose of NS	Score	No of refs	Results
Hoseini. HF (Iran)	2013	DB[1]-RCT[2]	8 weeks	Effect of NS[3] oil on BP in healthy adults	70 (35/35)	34-63	5 mL/day	24	47	Sig[4] reduction (P<0.001) in SBP[5] and DBP[6]
Dehkordi (Iran)	2008	DB-RCT	8 weeks	Effect of NS on BP in patients with mild hypertension	108 (36, 39/33)	35-50	200 mg/day and 400 mg/day (extract of NS)	24	43	Sig reduction (P<0.05) in SBP and DBP. Nonsig. change (P>0.05) in weight, TG,[7] and HDL[8]
Hoseini. MS (Iran)	2013	DB-RCT	3 month	Efect of NS oil in Type 2 diabetic Patients	70 (35/35)	34-63	5 ml/day	24	30	Sig reduction (P<0.05) in FBS[9], 2 h PPBG[10], HbA1C,[11], BMI,[12] and TC.[13] Nonsig. change (P>0.05) in TG, LDL,[14] and HDL
Qidwai (Pakistan)	2009	DB-RCT	6 weeks	Effect of NS on some blood parameters and body weight	73 (39/34)	≥18	1 g/day	24	39	Nonsig. change (P>0.05) in Lipid profile, FBS, BMI, BP, and WC[15]
Mohtashami (Iran)	2011	RCT	2 months	Effect of NS oil on blood glucose in healthy adults	70 (35/35)	25-60	5 mL/day	23	49	Sig. reduction (P<0.05) in FBS and HbA1c
Datau (Indonesia)	2010	DB-RCT	3 month	Effect of NS on some blood parameters and weight in obese men	39 (19/20)	30-45	1.5 g/day	22	45	Sig. reduction (P<0.001) in weight and WC Nonsig. change (P>0.05) in BP, FBS, TG, and HDL
Sabzghabaee (Iran)	2012	RCT	4 weeks	Effect of NS in treatment of hyperlipidemia	74 (37/37)	≥18	2 g/day	21	41	Sig. reduction (P<0.001) in TC., LDL, and TG. Nonsig. change (P>0.05) in FBS and HDL
Ibrahim R.M. (Malaysia)	2014	RCT	2 months	Effect of NS on some blood parameters in menopausal women	37 (19/18)	50-55	1 g/day	18	42	Sig. reduction (P<0.05) in TC., TG, LDL, and FBS. Nonsig. change (P<0.05) in BP and HDL
Najmi (North India)	2012	RCT	8 weeks	Effect of NS on some blood parameters in patients with poor glycemic control	80 (40/40)	40-60	500 mg/day	17	35	Sig. reduction (P<0.001) in FBS 2 h PPBG, HbA1c, and LDL. Nonsig. change (P>0.05) in TG and HDL
Najmi (North India)	2013	RCT	8 weeks	Effect of NS on BP in metabolic syndrome	90 (45/45)	40-60	500 mg/day	17	36	Sig. reduction (P<0.001) in SBP and DBP
Ibrahim R.M (Malaysia)	2014	RCT	2 months	Effect of NS on metabolic syndrome in menopausal women	35 (18/17)	45-60	1 g/day	17	34	Sig. reduction (P<0.05) in TC., LDL, TG, and FBS. Nonsig. change (P>0.05) in weight and HDL
Najmi (North India)	2007	RCT	6 weeks	Effect of NS oil on parameters of metabolic syndrome	161 (81/80)	40-60	5 mL/day	16	37	Sig. change (P<0.05) in LDL, FBS, and HDL Nonsig. reduction (P>0.05) in weight, BP, TC., TG, and WC
Bamosa (Saudi Arabia)	1997	CT[16]	2 weeks	Effect of NS on some blood parameters	16 (9/7)	Second year male medical students	2 g/day	16	46	Sig reduction (P<0.05) in FBS and TC. Nonsig. reduction (P>0.05) in TG
Shah (Pakistan)	2012	CT	6 weeks	Effect of NS on metabolic syndrome	159 (80/79)	40-60	500 mg/day	16	33	Sig. change (P<0.05) in FBS, LDL, and HDL Nonsig. reduction (P>0.05) in TC, weight, TG, BP, and WC
Elrehany (Egypt)	2012	CT	8 weeks	Effect of NS oil on patients with coronary artery disease and dyslipidemia	55 (40/15)	35-65	900 mg/day	15	44	Sig. change (P<0.001) in BP, TC., LDL, TG, and HDL
Haque (North India)	2011	RCT	6 weeks	Effect of NS oil as antiobesity therapy in metabolic syndrome	60 (30/30)	40-60	5 mL/day	15	38	Nonsig. change (P=?) in weight and WC
Najmi (North India)	2008	CT	6 weeks	Efect of NS oil on various parameters in metabolic syndrome	60 (30/30)	?	5 mL/day	14	32	Sig. reduction (P<0.05) in TC, LDL, and FBS. Nonsig. change (P>0.05) in TG, HDL, and WC
Ahmed (Egypt)	2012	CT	6 months	Effect of NS tea on glycemic control and lipid profile in type 2 diabetic patients	66 (41/25)	?	5 g/day (Extract of *N. sativa*)	14	31	Sig. change (P<0.001) in FBS, TC, LDL, TG, and HDL

1 = Double blind; 2 = Randomized clinical tiral; 3 = *Nigella sativa*; 4 = Significant; 5 = Systolic blood pressure; 6 = Diastolic blood pressure; 7 = Triglyceride; 8 = High-density lipoprotein; 9 = Fasting blood sugar; 10 = 2-hour Post Prandial Blood Glucose. 11 = Glycosylated hemoglobin. 12 = Body mass index. 13 = Cholesterol. 14 = Low-density lipoprotein. 15 = Waist circumference. 16 = Clinical trial

Table 3: Characteristics of included studies (quasi-experimental) (listed based on acquired score)

Author	Date of publication	Study design	Duration of study	Aims	*N* (case/control)	Age of subject (years)	Dose of NS	Score	No. of refs	Results
Bamosa (Saudi Arabia)	2010	CT (Noncontrol)	3 months	Effect of NS on glycemic control in patients with type 2 diabetes	68 (23, 26, 19)	18-60	1 2 3 g/day	19	27	Nonsig. change (P>0.05) in group with 1 g/day. Sig. reduction (P<0.05) in FBS, 2h PPBG, HbA1c in group with 2.3 g/day
Kaatabi (Saudi Arabia)	2012	CT (Non control)	3 months	Effect of NS on lipid profile in type 2 diabetic patients	71 (23, 26, 22)	18-60	1 2 3 g/day	19	29	Nonsig. change (P>0.05) in group with 1 g/day. Sig. change (P<0.05) in TC., TG, LDL, and HDL in group 2.3 g/day
Bilal (Pakistan)	2009	CT Noncontrol) (40-day NS 40-day placebo)	40 days	Effect of NS oil on some blood parameters in type 2 diabetic patients	41	30-60	0.7 g/day	18	28	Sig. reduction (P<0.001) in FBS
Ibrahim D.A (Yemen)	2011	CT (Noncontrol) 2 weeks NS 2 weeks washout 2 weeks oil fish	2 weeks	Effect of NS (in comparison fish oil) on blood glucose and lipid profile	18	23-31	500 mg/day	16	48	Sig. reduction (P<0.05) in FBS. Nonsig. change (P>0.05) in lipid profile
Bhatti (Pakistan)	2009	CT (Noncontrol)	2 months	Effect of NS on lipid profile in hyperlipidemic Patients	10	50-55	1 g/day	16	40	Sig. change (P<0.05) in TC., TG, LDL, and HDL

at the beginning of study, and the nausea disappeared at the second week of intervention.

In the other 8 trials, no notable liver or kidney side effects were observed. This was evidenced by laboratory tests done for liver and kidney functions.

Other articles (13 trials) did not detect any adverse effects of this plant.

DISCUSSION

In this systematic review we have tried to evaluate the effects of *N. sativa* supplementation on lipid profiles, glycemic factors, BP, and some of anthropometric indices (weight, BMI, and WC), of which a few are parameters of metabolic syndrome.

In many studies *N. sativa* could effectively change parameters in different patients and subjects, but in several trials these changes were not significant [refer to Table 2].

Lipid profiles constitute one of the most important factors that can be changed in many diseases and are used to evaluate conditions of the patients and subjects. In our review, changes in lipid profiles were different as in many trials *N. sativa* supplement could change these parameters significantly, but in some studies it could not. However, in 4 articles[29,31,40,44] all of parameters (TG, TC, LDL, and HDL) were affected significantly by *N. sativa*.

Several mechanisms are proposed to explain the hypolipidemic effect of *N. sativa*, including:

- Increase in cholesterol metabolism due to a rich source of polyunsaturated fatty acids.[50]
- Inhibition of lipid peroxidation and reduction in cholesterol synthesis in the liver by antioxidant factors such as phytosterols and flavonoids.[51]
- Reduction insulin resistance and dyslipidemia throughout antioxidative action of thymoquinone.[52]
- Increase in the secretion of cholesterol in the bile and hence excretion in feces.[53]
- Reduction of serum TG due to presence of nigellamin that act like a clofibrate.[54]
- Regulation of cholesterol synthesis through effect on key enzyme HMG-COA reductase (Hydroxy Methyl Glutaryle – COA).[55]

Although some trials had not reported any significant change in lipid profiles caused by *N. sativa*, the researcher proposed several factors, such as increased dropouts and small sample size[39] or different characteristic of patients.[30]

In the other studies, the reasons for nonsignificant change in these parameters are not reported. However, it is speculated that the factors that are effective include:

- Different characteristic of patients in study.[32,33,37,49]
- Small dose of supplement.[33,43,47]
- Short duration of intervention.[37,47]

Glycemic control involving factors such as FBS and HbA1c are useful parameters in the detection and control of diabetes and increased blood glucose in the subjects. Of course, HbA1c is used to evaluate blood sugar in the past several weeks. Our review revealed that these factors are affected in many trials and *N. sativa* could reduce glycemic factors significantly. However, in a few studies this effect was not seen.[39,41,49]

It is proposed that reduction of FBS and HbA1c by *N. sativa* supplementation is related to the following:

- Reduction in oxidative stress and maintenance of the integrity of pancreatic b-cells that lead to increased blood insulin level.[56,57]
- Presence of thymoquinone with antioxidant activity.[58]
- Activation of insulin receptors and improvement in tissue sensitivity to insulin.[59]
- Decreased gluconeogenesis in the liver.[60]
- Reduction in glucose absorption from the intestine.[61]

In 3 trials that did not demonstrate any hypoglycemic effect of *N. sativa*, some reasons were proposed, including: small sample size[39] and short-term duration of intervention, and probably change in diet or exercise.[41]

In 1 trial[45] any reason was reported but it was speculated that small sample size and low dose of supplement were effective.

BP is one of the most important parameters that is evaluated in many studies (9 trials). In 4 studies,[36,43,44,46] the antihypertensive effect of *N. sativa* was demonstrated. However, in 5 trials this effect was not significant.[33,37,39,42,49]

The authors proposed several mechanisms for lowering BP using *N. sativa* supplementation, including the following:

- Antioxidant activity of thymoquinone, polyphenols, and flavonoids in *N. sativa* that cause nitric oxide production and vasodilator effect.[62]
- Presence of linoleic acid that affects ionic fluxes across the vascular endothelial cells.[63]
- Presence of oleic acid that regulates lipid structure in membrane and control G-protein.
- Mediated signaling that leads to lowering of BP.[64]
- Calcium channel-blocking activity by *N. sativa*.[65]
- Inhibition of angiotensin-converting enzyme by flavonoids.[66]

In some trials that did not reveal any significant effect of *N. sativa* on BP, the researchers did not detect any obvious reasons.[33,37,39,42,49] Only in 1 trial, the author reported a small sample size and limited duration of the intervention.[39] It seems that in other studies there are different reasons, such as small sample size,[42,49] low dose of supplement,[33,42,49] and short duration of intervention.[33,37]

With regard to anthropometric parameters (weight and WC), there are remarkable results. Only in 2 trials was the effect of *N. sativa* in reducing weight or WC statistically significant.[30,49] However, in 7 studies, these effects were not found.[32,33,34,37,38,39,43]

It has been proposed that the petroleum extract of *N. sativa* has a slight appetite-reducing property[67] and also has antiobesity action because of the presence of lipase enzyme.[68]

While these 7 studies had no significant effects, only 1 trial[39] had reported a small sample size as a reason. It seems that in other studies (6 trials), several factors were effective, including low doses of the supplement[33,34,39,43] and the short duration of intervention.[33,37,38,39]

Limitation

The most important limitation in our systematic review was difficulty in finding the full texts of many published papers. Further, we included only English-language articles and clinical trials in this review and not other studies.

CONCLUSION

This systematic review on 23 studies demonstrated that *N. sativa* supplement in different doses and durations can change various clinical and biochemical parameters, including lipid profiles, glycemic factors, BP, and some anthropometric indices in humans. However, the effect of this supplement is more pronounced on levels of TC, LDL, FBS, and HbA1c than on TG, HDL, BP, weight, and WC.

Therefore, it is suggested that consumption of *N. sativa* supplementation be considered as a complementary treatment protocol for many diseases, especially metabolic disorders.

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Conflicts of interest

There are no conflicts of interest.

AUTHOR'S CONTRIBUTION

AM contributed in the preparation of the work and conducting the study and MHE (as Corresponding author) contributed in the revising of the draft and approval of the final version of manuscript.

REFERENCES

1. Ali BH, Blunden G. Pharmacological and toxicological properties of *Nigella sativa*. Phytother Res 2003;17:299-305.
2. Sayed M. Traditional medicine in health care. J Ethnopharmacol 1980;2:19-22.
3. Shrivastava RM, Agrawal RC, Parveen ZJ. A review on therapeutic applications of *Nigella sativa*. J Chem Chem Sci 2011;1:241-8.
4. Ali K, Hasanah M, Ghazali A, Yassoralipour Y, Ali G. Physicochemical characteristics of nigella seed (*Nigella sativa* L.) oil as affected by different extraction methods. J Am Oil Chem Soc 2011;88:533-40.
5. al-Awadi F, Fatania H, Shamte U. The effect of a plants mixture extract on live gluconeogenesis in streptozosin induced diabetic rats. Diabetes Res 1991;18:163-8.
6. Zaoui A, Cherrah Y, Alaoui K, Mahassine N, Amarouch H, Hassar M. Effects of *Nigella sativa* fixed oil on blood homeostasis in rat. J Ethnopharmacol 2002;79:23-6.
7. Gilani AH, Shaheen F, Shakir T. Thymol lowers blood pressure through blockade of calcium channels. Fundam Clin Pharmacol 2001;15:8P163.
8. Badary OA, Abdel-Naim AB, Abdel-Wahab MH, Hamada FM. The influence of thymoquinone on doxorubicin-induced hyperlipidemic nephropathy in rats. Toxicology 2000;143:219-26.
9. Al-Ghamdi MS. The anti-inflammatory, analgesic and antipyretic activity of *Nigella sativa*. J Ethnopharmacol 2001;76:45-8.
10. Parhizkar S, Latif LA, Rahman SA, Dollah MA. Preventive effect of *Nigella sativa* on metabolic syndrome in menopause induced rats. J Med Plants Res 2011;5:1478-84.
11. Nickavar B, Mojab F, Javidnia K, Amoli MA. Chemical composition of the fixed and volatile oils of *Nigella sativa* L. from Iran. Z Naturforsch C 2003;58:629-31.
12. Salama RH. Hypoglycemic effect of lipoic acid, carnitine and *Nigella Sativa* on diabetic rat model. Int J Health Sci (Qassim) 2011;5:126-34.
13. Khattab MM, Nagi MN. Thymoquinone supplementation attenuates hypertension and renal damage in nitric oxide deficient hypertensive rats. Phyto ther Res 2007;21:410-4.
14. Zaoui A, Cherrah Y, Lacaille-Dubois MA, Settat A, Amarouch H, Hassar M. Diuretic and hypotensive effects of Nigella sativa in the spontaneously hypertensive rat. Therapie 2000;55:379-82.
15. el Tahir KE, Ashour MM, al-Harbi MM. The cardiovascular actions of the volatile oil of the black seed (*Nigella sativa*) in rats: Elucidation of the mechanism of action. Gen Pharmacol 1993;24:1123-31.
16. Tsimidou M, Papadopoulos G, Boskou B. Determination of phenolic compounds in virgin olive oil by reversed-phase HPLC with emphasis on UV detection. Food Chem 1992;44:53-60.
17. Mahfouz M, El-Dakhakhny M. Some chemical and pharmacological properties of the new anti-asthmatic drug, Nigellone. Egypt Pharm Bull 1960;42:411-24.
18. Toppozada HH, Mazloum HA, el-Dakhakhny M. The antibacterial properties of the *Nigella sativa* l. Seeds. Active principle with some clinical applications. J Egypt Med Assoc 1965;48(Suppl):187-202.
19. Fararh KM, Atoji Y, Shimizu Y, Takewaki T. Isulinotropic properties of *Nigella sativa* oil in Streptozotocin plus Nicotinamide diabetic hamster. Res Vet Sci 2002;73:279-82.
20. Kanter M, Meral I, Yener Z, Ozbek H, Demir H. Partial regeneration/proliferation of the beta cells in the islets of Langerhans by *Nigella sativa* L. in streptozotocin-induced diabetic rats. Tohoku J Exp Med 2003;201:213-9.
21. Khanam M. Dewan F. Effects of the crude and the n-hexane extract of *Nigella sativa* Linn (kalajira) upon diabetic rats. Bangla J Pharmacol 2008;4:17-20.
22. el-Dakhakhny M, Mady NI, Halim MA. *Nigella sativa* L. Oil protects against induced hepatotoxicity and improves serum lipid profile in rats. Arzneimittelforschung 2000;50:832-6.
23. Qidwai W, Ashfaq T. Effect of dietary supplementation of black seed (*N. Sativa* L.) on lipid profile of patients suffering from diabetes. Antiinflamm Antiallergy Agents Med Chem 2014;13:3-8.
24. Leong XF, Rais Mustafa M, Jaarin K. Nigella sativa and its protective role in oxidative stress and hypertension. Evid Based Complement Alternat Med 2013;2013:120732.
25. Burits M, Bucar F. Antioxidant activity of *Nigella sativa* essential oil. Phytother Res 2000;14:323-8.
26. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998;52:377-84.
27. Bamosa AO, Kaatabi H, Lebdaa FM, Elq AM, Al-Sultanb A. Effect of *Nigella sativa* seeds on the glycemic control of patients with type 2 diabetes mellitus. Indian J Physiol Pharmacol 2010;54:344-54.
28. Bilal A, Masud T, Uppal AM, Naveed AK. Effects of *Nigella sativa* oil on some blood parameters in Type 2 diabetes mellitus patients. Asian J of Chemistry 2009;21:5373-81.
29. Kaatabi H, Bamosa AO, Lebda FM, Al Elq AH, Al-Sultan AI. Favorable impact of *Nigella sativa* seeds on lipid profile in type 2 diabetic patients. J Family Community Med 2012;19:155-61.
30. Hoseini MS, Mirkarimi SA, Amini M, Mohtashami R, Kianbakht S, Fallah Hoseini H. Effects of *Nigella sativa* L. seed oil in type II diabetic Patients: A randomized, double-blind, placebo-controlled clinical trial. J Med Plants 2013;12:93-9.
31. Ahmed MM, El-Shamy KA, El-Nabarawy SK, Elbaiomy MA, El-Qattan GM. *Nigella sativa* tea improved serum paraoxonase-1 activity, glycemic control and lipid profile in type 2 diabetes mellitus. J Appl Sci Res 2012;8:5897-902.
32. Najmi A, Nsiruddin M, Khan RA, Haque SF. Effect of *Nigella sativa* oil on various clinical and biochemical parameters of insulin resistance syndrome. Int J Diabetes Dev Ctries 2008;28:11-4.
33. Shah AS, Khan GM, Badshah A, Shah SU, Shah KU, Mirza SA, *et al*. *Nigella sativa* provides protection against metabolic syndrome. Afr J Biotechnol 2012;11:10919-25.
34. Ibrahim RM, Hmdan NS, Ismail M, Saini SM, Abd Rashid SN, Abd Ltiff L, *et al*. Protective effects of *Nigella sativa* on metabolic syndrome in menopausal women. Adv Pharm Bull 2014;4:29-33.
35. Najmi A, Nsiruddin M, Khan RA, Haque SF. Therapeutic effect of *Nigella sativa* in patients of poor glycemic control. Asian J Pharm Clin Res 2012;5:224-8.
36. Najmi A, Nsiruddin M, Khan RA, Haque SF. Indigenous herbal product *Nigella sativa* proved effective as an antihypertensive in metabolic syndrome. Asian J Pharm Clin Res 2013;6:6-4.
37. Najmi A, Haque S, Khan R, Nasiruddin M. Therapeutic effect of *Nigella Sativa* oil on different clinical and biochemical parameters in metabolic syndrome. The Int J of pharm 2007;5:13.
38. Haque SH, Nasiruddin M, Najmi A. Indigenous herbal product *Nigella sativa* proved effective as an anti-obesity therapy in metabolic syndrome. Int J Med Res 2011;1:173-6.

39. 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;15:639-44.
40. Bhatti IU, Rehman FU, Khan MA, Marwat SK. Effect of prophetic medicine kalonji (*Nigella sativa* l) on lipid profile of human beings: An *in vivo* approach. World Appl Sci J 2009;6:1053-7.
41. Sabzghabaee AM, Dianatkhah M, Sarrafzadegan N, Asgary S, Ghannadi A. Clinical Evaluation of *Nigella Sativa* seeds for the treatment of hyperlipidemia: A randomized, placebo controlled clinical trial. Med Arch 2012;66:198-200.
42. Ibrahim RM, Hamdan NS, Mahmud R, Imam MU, Saini SM, Rashid SN, *et al*. A randomised controlled trial on hypolipidemic effects of *Nigella Sativa* seeds powder in menopausal women. J Transl Med 2014;12:82.
43. Dehkordi FR, Kamkhah AF. Antihypertensive effect of *Nigella sativa* seed extract in patients with mild hypertension. Fundam Clin Pharmacol 2008;22:447-52.
44. Elrehany M, Elbawb Elsaid ME, Younis HA, Mhmoud AM. Therapeutic effect of *Nigella sativa* on patients with coronary artery disease. AAMJ 2012;10:12-25.
45. Bamosa AO, Basil A, Sowayan AA, Sowayan SA. Effect of oral ingestion of *Nigella sativa* seeds on some blood parameters. Saudi Pharma J 2007;2:126-9.
46. Fallah Huseini H, Amini M, Mohtashami R, Ghamarchehre ME, Sadeqhi Z, Kianbakht S, *et al*. Blood pressure lowering effect of *Nigella sativa* L. seed oil in healthy volunteers: A randomized, double-blind, placebo-controlled clinical trial. Phytother Res 2013;27:1849-53.
47. Ibrahim DA. Comparative study between plant and animal sources of omega-3 fatty acid in their potential role of regulating blood glucose and lipid Profile in Healthy Volunteers. Yemeni J Med Sci 2011;5:7-14.
48. Mohtashami R, Amini M, Fallah Huseini H, Ghamarchehre M, Sadeqhi Z, Hajiagaee R, *et al*. Blood glucose lowering effects of *Nigella Sativa* L. seeds oil in healthy volunteers: A randomized, double-blind, placebo-controlled clinical trial. J Med Plants 2011;10:90-4.
49. Datau EA, Wardhana, Surachmanto EE, Pandelaki K, Langi JA, Fias. Efficacy of *Nigella Sativa* on serum free testosterone and metabolic disturbances in central obese male. Acta Med Indones 2010;42:130-4.
50. Padhye S, Banerjee S, Ahmad A, Mohammad R, Sarkar FH. From here to eternity-the secret of pharaohs: Therapeutic potential of black cumin seeds and beyond. Cancer Ther 2008;6:495-510.
51. de Jong A, Plat J, Mensink RP. Metabolic effects of plant sterols and stanols (Review). J Nutr Biochem 2003;14:362-9.
52. Ismail M, Al-Naqeep G, Chan KW. *Nigella sativa* thymoquinonerich fraction greatly improves plasma antioxidant capacity and expression of antioxidant genes in hypercholesterolemic rats. Free Radic Biol Med 2010;48:664-72.
53. Ibraheim Z. Effect of *Nigella sativa* seeds and total oil on some blood parameters in female volunteers. Saudi Pharm J 2002;10:54-9.
54. Morikawa T, Xu F, Ninomiya K, Matsuda H, Yoshikawa M. Nigellamines A3, A4, A5, and C, new dolabellane-type diterpene alkaloids, with lipid metabolism-promoting activities from the Egyptian medicinal food black cumin. Chem Pharm Bull (Tokyo) 2004;52:494-7.
55. Al-Naqeep G, Ismail M. Effects of thymoquinone rich fraction and thymoquinone on plasma lipoprotein level and hepatic low-density lipoprotein receptor and 3-hydroxy-3-methylglutaryl coenzyme a Reductase gene expression. J Funct Foods 2009;1:298-303.
56. Alsaif MA. Effect of *N. Sativa* oil on Impaired glucose tolerance and insulin insensitivity induced by high-fat-diet and turpentine-induced trauma. Pak J Biol Sci 2008;11:1093-9.
57. Abdelmeguid NE, Fakhoury R, Kamal SM, Al Wafai RJ. Effects of *Nigella sativa* and hymoquinone on biochemical and subcellular changes in pancreatic β-cells of streptozotocin induced diabetic rats. J Diabetes 2010;2:256-66.
58. Geng D, Zhang S, Lan J. Analysis on chemical components of volatile oil and determination of thymoquinone from seed of *Nigella glandulifera*. Zhongguo Zhong Yao Za Zhi 2009;34:2887-90.
59. Le PM, Benhaddou-Andaloussi A, Elimadi A, Settaf A, Cherrah Y, Haddad PS. The petroleum ether extract of Nigella sativa exerts lipid-lowering and insulin-sensitizing actions in the rat. J Ethnopharmacol 2004;94:251-9.
60. Fararh KM, Shimizu Y, Shiina T, Nikami H, Ghanem MM, Takewaki T. Thymoquinone reduces hepatic glucose production in diabetic hamsters. Res Vet Sci 2005;79:219-23.
61. Meddah B, Ducroc R, El Abbes Faouzi M, Eto B, Mahraoui L, Benhaddou-Andaloussi A, *et al*. *Nigella sativa* inhibits intestinal glucose absorption and improves glucose tolerance in rats. J Ethnopharmacol 2009;121:419-24.
62. Andriambeloson E, Magnier C, Haan-Archipoff G, Lobstein A, Anton R, Beretz A, *et al*. Natural dietary polyphenolic compounds cause endothelium-dependent vasorelaxation in rat thoracic aorta. J Nutr 1998;128:2324-33.
63. el Ashry A, Heagerty AM, Ollerenshaw JD, Thurston H. The effect of dietary linoleic acid on blood pressure and erythrocyte sodium transport. J Hum Hypertens 1989;3:9-15.
64. Terés S, Barceló-Coblijn G, Benet M, Alvarez R, Bressani R, Halver JE, *et al*. Oleic acid content is responsible for the reduction in blood pressure induced by olive oil. Proc Natl Acad Sci U S A 2008;105:13811-6.
65. Bamosa AO, Ali BA, al-Hawsawi ZA. The effect of thymoquinone on blood lipids in rats. Indian J Physiol Pharmacol 2002;46:195-201.
66. Actis-Goretta L, Ottaviani JI, Fraga CG. Inhibition of angiotensin converting enzyme activity by flavanol-rich foods. J Agric Food Chem 2006;11:229-34.
67. Le PM, Benhaddou-Andaloussi A, Elimadi A, Settaf A, Cherrah Y, Haddad PS. The petroleum ether extracts of *Nigella sativa* seeds exert insulin sensitizing and lipid lowering action in rats. J Ethnopharmacol 2004;94:251-9.
68. Akova A, Ustun G. Activity and adsorption of lipase from Nigella sativa seeds. Biotechnol Lett 2004;22:355-9.