

Effect of *Nigella sativa* supplementation over a one-year period on lipid levels, blood pressure and heart rate in type-2 diabetic patients receiving oral hypoglycemic agents: nonrandomized clinical trial

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BACKGROUND: Diabetic patients with hypertension and dyslipidemia are at a high risk of cardiovascular complications.

OBJECTIVES: To determine the effect of *Nigella sativa* supplementation on the lipid profile, mean arterial pressure, and heart rate in persons with type 2 diabetes on oral hypoglycemic agents (OHA).

DESIGN: Single-blind, nonrandomized.

SETTING: Diabetes clinic of a university hospital in Saudi Arabia.

PATIENTS AND METHODS: Type-2 diabetic patients were recruited by purposive sampling and assigned to treatment or control at the discretion of the investigator with the patient blinded to treatment. Before the intervention and every 3 months thereafter until the end of the treatment period, the following parameters were measured: triglycerides (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), and body mass index (BMI). Results at the baseline and each subsequent visit were compared between the two groups.

MAIN OUTCOME MEASURE(S): Lipid and cardiovascular parameters, and BMI.

RESULTS: Fifty-seven patients were assigned to receive *N sativa* 2 g daily for one year and 57 were assigned to receive an identical regimen of placebo, along with OHA. A significant decrease in HDL-C and increase in the TC/HDL-C and LDL-C/HDL-C ratios were seen in the control group. The *N sativa* group had a significant decline in TC, LDL-C, TC/HDL-C and LDL-C/HDL-C ratios, compared with the respective baseline data and the control group. HDL-C was significantly elevated in the *N sativa* group. The control group showed a significant elevation in MAP. The *N sativa* group had a significant reduction in SBP, DBP, MAP and HR and a significant decrease in DBP, MAP and HR as compared with the control group.

CONCLUSION: *N sativa* supplementation improves total cholesterol, mean arterial pressure and heart rate in type 2 diabetes patients on oral hypoglycemic agents.

LIMITATIONS: There were 9 subjects in each group lost to follow up; thus the sample size could not be maintained as per the sample size calculation. The study was nonrandomized and thus there was a possibility of allocation bias. (Clinical trial registration number: CTRI/2013/06/003781, Clinical Trial Registry of India).

Diabetes mellitus is a major and growing public health issue worldwide, but especially in Saudi Arabia.¹ Diabetes is associated with cardiovascular disease (CVD) risk factors such as dyslipidemia, hypertension and obesity, among others, which are established predictors of adverse cardiovascular outcome.^{2,3} The altered composition of lipoproteins and lipids in type 2 diabetic patients, called diabetic dyslipidemia, is characterized by elevated levels of triglyceride and cholesterol-rich very low density lipoprotein with reduced levels of high-density lipoprotein cholesterol (HDL-C).⁴ It has been suggested that lowering lipid levels intensively might immediately reduce the likelihood of CVD events arising in diabetic patients.⁵

Remarkably, hypertension occurs approximately twice as often in patients with diabetes compared with non-diabetic persons. In addition, up to 75% of CVD in patients with diabetes may be attributed to hypertension.⁶ Moreover, diastolic heart failure has been recognized as a major adverse manifestation of hypertension and diabetes,⁷ leading to recommendations for more aggressive blood pressure control in diabetic persons with coexistent hypertension.⁶ The use of herbal drugs as complementary medicine is prevalent worldwide and is gaining popularity. *Nigella sativa* is a widely used medicinal plant throughout the world with a long history of use of the raw seeds as well as oil in medicines and food.⁸

The lipid lowering effect of *N sativa* powdered seeds⁹ and its extract¹⁰ has been observed in normal rats. Moreover, the protective effects of thymoquinone (TQ), the active ingredient of *N sativa*, on development of atherosclerosis have been reported in cholesterol-fed rabbits.^{11,12} Likewise, strong evidence supports the usefulness of TQ in the prevention of CVD risk parameters in rats fed an atherogenic suspension.¹³ Other studies explored the hypotensive effect of *N sativa* seed extract in spontaneously hypertensive rats¹⁴ and in humans with mild hypertension.¹⁵ *N sativa* also has a potential to reduce elevated heart rate induced by the toxic effect of alloxan-induced diabetes in rabbits¹⁶ and cadmium-treated rats.¹⁷

Despite the evidence in favor of *N sativa* effects on major cardiovascular risk factors in different animal models, convincing therapeutic strategy and strict risk factor control by *N sativa* are still lacking in human diabetics. A recent systematic review and meta-analysis of 17 randomized controlled trials concluded that *N sativa* significantly decreases plasma lipid concentration (total cholesterol, LDL, and TG) whereas HDL-C increased with the powdered form only.¹⁸ The same effect on lipids was observed in centrally obese men

treated with *N sativa* for 3 months.¹⁹ In the past our group has found a significant decrease in lipids²⁰ and hemodynamic parameters²¹ after three months of treatment with *N sativa* seeds in type 2 diabetic patients. We concluded from that study that a prolonged study was required to establish the effect and safety of *N sativa* supplementation. Therefore, we planned this study to evaluate the effect of long-term (one year) *N sativa* supplementation, as adjuvant therapy, on the lipid profile, blood pressure and heart rate in type 2 diabetic patients on oral hypoglycemic agents (OHA).

PATIENTS AND METHODS

This study was conducted at the Department of Physiology, College of Medicine, University of Dammam while the patients were recruited from the diabetes clinic of King Fahd Hospital of the University of Dammam, Saudi Arabia. The study was approved by the Research and Ethical committee of the University of Dammam and registered as a clinical trial in the clinical trial registry of India (Clinical trial registration number: CTRI/2013/06/003781, Clinical Trial Registry of India, Website URL: <http://ctri.nic.in>).

Sample size was calculated by software G*Power (University of Dusseldorf, Germany, version 3.1.9.2, <http://www.gpower.hhu.de/en.html>)²² to be 57 for each of the two the groups (N=114). The parameters used for calculation were α error probability=0.05, power 1- β , error probability=0.95, effect size=0.62 (based on the closely matching contemporary studies) and allocation ratio (N2/N1)=1, computed for independent sample t test for two groups.

Patients with type 2 diabetes were recruited by purposive sampling. Allocation to the groups was done at the discretion of the investigator who matched the male-to-female ratio, age, duration of diabetes and body mass index (BMI) in the two groups (**Figure 1**).

The criteria for inclusion was poorly controlled type 2 diabetes (determined by two readings of HbA1c of more than 7% taken three months apart, 18-60 years of age, and regular use standardized oral medications [glibenclamide, metformin or rosiglitazone]). Criteria for exclusion were HbA1c in excess of 9%, insulin therapy, BMI in excess of 40kg/m², triglyceride (TG) more than 400 mg/dL, any other reason for deranged lipids, major cardiovascular disease, hepatic disorder, renal disorder, pregnancy/lactation and compliance <90% or change in medications during the study period. Informed consent, which included full information about the purpose and the duration of the study, was taken from all the subjects in writing. The subjects were told that they could leave the study at any time.

Intervention

Nigella sativa seeds (Bioextract [Pvt] Ltd, Sri Lanka) were provided in the form of 500 mg oral capsules. A dose of 2 grams/day was used. This dose was already determined to be effective in reducing blood glucose in a previous study published by our department.²³ The placebo was an activated charcoal capsule (260 mg), supplied by Arkopharma Pharmaceutical Laboratories Carros, France that closely matched the color and size of the *N sativa* capsules. The supplementation in two divided doses daily, along with the regular standardized treatment continued for one year.

The baseline data including age, sex and duration of disease was recorded before the start of treatment.

Clinical and analytical methods

Lipid parameters; triglycerides (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C), as well as BMI and hemodynamic parameters; heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were mea-

sured before intervention (baseline) and every three months thereafter until the end of the study period. Also, TC/HDL-C ratio and LDL-C/HDL-C were calculated. In addition, fasting blood glucose (FBG), glycosylated hemoglobin (HbA1c), renal and liver function tests and complete blood count were also carried out at baseline and at all the follow up visits. Patients were asked not to smoke or engage in physical activity for 30 minutes before the above measurements and drawing of blood. Patients were asked to report any adverse sign or symptom via phone (numbers were provided) to make decisions about discontinuation of medicine.

Blood samples were collected, after at least 12 hours of fasting, into plain tubes (without anticoagulant) and allowed to clot. They were then centrifuged at 3000 rpm for 8 min for separation of the serum. Serum was stored and kept frozen at -20°C for up to 1 week until used for determination of TG, TC, and HDL-C. The kits were supplied by Dade Behring, Germany. Assays were performed according to the manufacturer's instructions, using the automated assay analyzer (Dimension Clinical Chemistry System, Germany). LDL-C was calculated using the Friedewald formula.²⁴

Blood pressure was measured in the sitting position with the arm supported at the level of the heart, after 10 minutes of rest, with a mercury sphygmomanometer by the auscultatory method. Blood pressure readings were based on the average of two independent measurements taken 5 minutes apart. HR at rest was determined by counting the radial pulse for one minute. The mean arterial pressure (MAP) was calculated by formula (MAP=diastolic pressure + 1/3 pulse pressure).

Statistical analysis

Statistical analyses were performed with SPSS version 19 (IBM, Armonk, NY, USA). Means and standard deviations (SD) were calculated. Comparison between the two groups (control and NS) was done using an independent samples t test at the baseline, 3 months, 6 months, 9 months and 12 months. *P* value was considered significant if *P* ≤ .05. The TREND statement (Transparent Reporting of Evaluations with Nonrandomized Designs) was used in the preparation of the manuscript.

RESULTS

Subjects (n=114, 63 males and 51 females) were non-randomly assigned to a placebo (control) (n=57, 30 males and 27 females) or *N sativa* (n=57, 33 males and

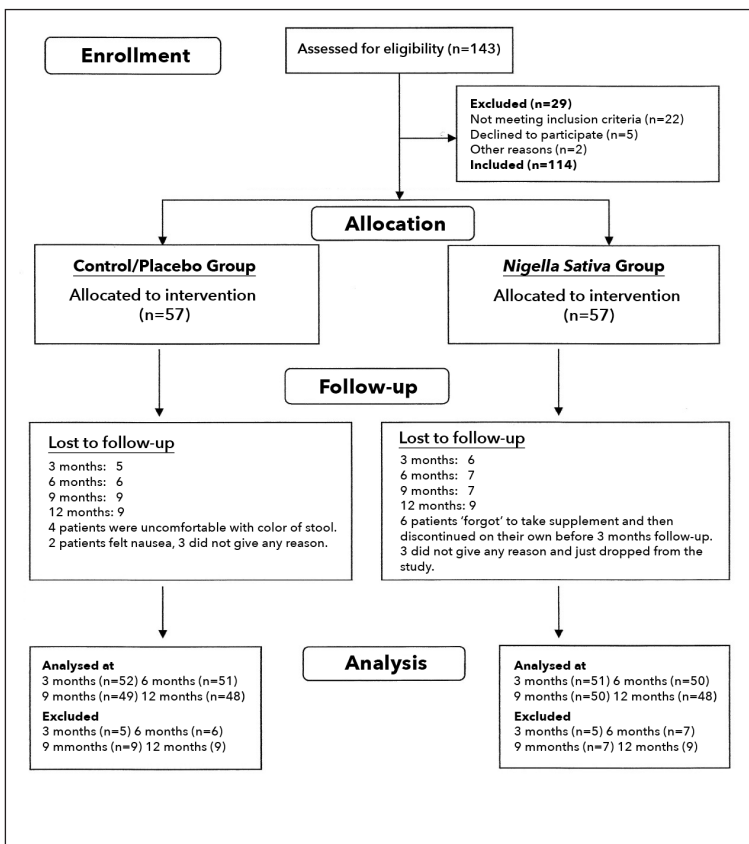


Figure 1. Flow diagram for allocation of patients.

24 females) (**Figure 1**). The two groups were of similar age, duration of disease, BMI, fasting blood glucose (FBG) and hemoglobin A1C (HbA1c) at baseline (**Table 1**). Other pretreatment baseline data did not differ significantly (**Tables 2 and 3**). Differences in TG and HDL-C were nonsignificant between the two groups at all timepoints (**Table 2**). TC was significantly lower in the *N sativa* group at 6, 9 and 12 months. Likewise, LDL-C was significantly less in the *N sativa* group as compared with the control group at 3 and 6 months. TC/HDL-C ratio was significantly less in the *N sativa* group at 6 and 9 months as compared with the control group. Likewise, LDL-C/ HDL-C was significantly less in the *N sativa* group at 6 months as compared with the control group. BMI was not significantly different in any of the two groups, therefore the intergroup and intragroup differences were non-significant (**Table 3**). HR was significantly ($P<.01$) less in *N sativa* group as compared with the control group at 3, 6, 9 and 12 months. SBP was not significantly different between the control and *N sativa* groups. DBP showed a significant difference between the control and *N sativa* groups at the 9th and 12th month. MAP was significantly different at the 12th month between the two groups. All patients tolerated the treatment well and reported no adverse effects throughout the study period. Furthermore, all blood tests related to renal and liver functions and complete blood count were normal in all readings taken during the one-year treatment with *N sativa*.

DISCUSSION

In the present study, *N sativa* supplementation for one year in patients with type 2 diabetes taking OHA was effective in lowering total cholesterol, LDL, blood pressure and heart rate. This reflects a potential protective role against CVD risks associated with diabetes. A recent study reported that immediate management of lipid levels after diagnosis of an abnormality correlated significantly with reduction in CVD events arising in diabetic patients with moderate or severe myocardial ischemia.⁵ In addition, it is known that a reduction in blood pressure by antihypertensive drugs is associated with a major decrease in cardiovascular morbidity and mortality.²⁵

In the present investigation, patients receiving *N sativa* seeds displayed a significant decrease in TC, LDL-C and the calculated lipid ratios (TC/HDL-C and LDL-C/HDL-C) (compared with the control group). In addition, HDL-C was higher than baseline values in the *N sativa* group. These results confirm the lipid lowering and antiatherogenic lipoprotein pattern activities

of *N sativa* seeds previously observed in patients with stable coronary artery disease²⁶ and in type 2 diabetic patients.²⁰ Another study was conducted in patients with hypercholesterolemia. They received 2 g *N sativa* per day for 4 weeks. This resulted in a significant decrease in TG, TC, LDL-C; however, it indicated that *N sativa* has no beneficial effects on fasting blood sugar and HDL-C.²⁷ Moreover, a nonsignificant reduction in lipids has been reported in adults who received powdered *N sativa* seeds¹⁸ and in men with central obesity treated with *N sativa* for 3 months.¹⁹

HDL-C levels are known to be inversely associated with prevalence of coronary artery disease.²⁸ However, not all therapies that increase HDL-C reduce CVD events, leading to the conclusion that targeting both HDL-C and LDL-C leads to greater benefit for CVD and clinical events.²⁹ Therefore, the increase in HDL-C with pronounced reduction in LDL-C, TC/HDL-C ratio and LDL-C/HDL-C ratios, seen in the present study, points to improvement in the lipoprotein components towards a non-atherogenic pattern. This highlights the efficacy of *N sativa* seeds as an ameliorating adjuvant for the CVD risks in type 2 diabetics on OHA. In support of these results is an animal study, in which feeding hypercholesterolemic rabbits with *N sativa* either in powder or oil forms was shown to significantly reduce TC and LDL-C levels and enhance HDL-C levels, indicating hypocholesterolemic and antiatherogenic cardioprotective properties of *N sativa*.³⁰

The significant decline in SBP, DBP, MAP and HR, demonstrated in this study is similar to results in two previous studies, one on rats and the other on humans.^{14,15} MAP was reduced by 22% in spontaneously hypertensive rats treated with *N sativa* extract.¹⁴ Oral supplementation with *N sativa* seed extract in patients with mild hypertension reduced both SBP and DBP in a dose-dependent manner.¹⁵ However, nonsignificant reductions in SBP and DBP have been reported

Table 1. Baseline demographic and clinical data.

Variables	Control (n=57)	<i>N sativa</i> (n=57)	P
Age (years)	46.12 (6.41)	46.82 (8.63)	.62
Duration of disease (years)	5.95 (4.33)	7.24 (3.81)	.09
Body mass index (kg/m ²)	31.83 (3.93)	30.47 (3.99)	.07
Fasting blood glucose (mg/dL)	180.9 (41.07)	195.9 (47.41)	.07
Hemoglobin A1C (%)	8.23 (0.90)	8.56 (0.90)	.06

Values are mean and standard deviation. Statistical method was the independent sample 't' test.

in males with central obesity receiving *N sativa* for 3 months compared to the controls.¹⁹ Differences in methodology and the type of subjects under study could account for this discrepancy.

Earlier results are consistent with our results, as in-

dicated by a decrease in the elevated heart rate induced by a toxic effect in (alloxan-induced) diabetic rabbits¹⁶ and in cadmium-treated rats¹⁷ treated with extract of *N sativa*. An in vitro study also showed a potent inhibitory effect of aqueous and macerated ex-

Table 2. Lipid profile at different treatment durations, between the control and *Nigella sativa* groups.

Variables (Mean ± SD)	Treatment duration	Control	<i>N sativa</i>	P value
TG (mg/dL)	Baseline	180.82 (124.14) (57)	170.87 (102.19) (57)	.64
	3 months	185.82 (111.09) (52)	168.35 (92.38) (51)	.38
	6 months	193.49 (110.28) (51)	167.06 (108.72) (50)	.22
	9 months	184.02 (115.19) (48)	162.34 (85.02) (50)	.29
	12 months	189.72 (114.99) (48)	169.62 (102.60) (48)	.36
TC (mg/dL)	Baseline	195.63 (46.30) (57)	194.19 (40.58) (57)	.86
	3 months	199.30 (45.84) (52)	185.56 (40.94) (51)	.11
	6 months	200.94 (43.31) (51)	177.64 (41.24) (50)	.007
	9 months	195.64 (34.54) (48)	180.18 (42.99) (50)	.05
	12 months	199.27 (39.29) (48)	180.66 (41.91) (48)	.02
LDL-C (mg/dL)	Baseline	122.98 (33.12) (57)	126.49 (33.91) (57)	.57
	3 months	127.98 (30.02) (52)	114.23 (35.29) (51)	.03
	6 months	128.62 (35.93) (51)	107.14 (36.48) (50)	.004
	9 months	120.58 (27.73) (48)	115.34 (38.50) (50)	.44
	12 months	120.72 (26.96) (48)	114.25 (34.62) (48)	.30
HDL-C (mg/dL)	Baseline	42.45 (10.05) (57)	42.54 (43.01) (57)	.96
	3 months	42.21 (9.83) (52)	43.01 (10.36) (51)	.68
	6 months	41.70 (8.41) (51)	42.68 (10.66) (50)	.61
	9 months	43.25 (11.13) (48)	45.02 (10.67) (50)	.42
	12 months	43.79 (9.81) (48)	44.02 (10.45) (48)	.91
TC/HDL-C	Baseline	4.72 (1.21) (57)	4.76 (1.31) (57)	.88
	3 months	4.88 (1.32) (52)	4.53 (1.39) (51)	.19
	6 months	4.95 (1.26) (51)	4.38 (1.33) (50)	.02
	9 months	4.70 (1.07) (48)	4.16 (1.22) (50)	.02
	12 months	4.75 (1.23) (48)	4.27 (1.40) (48)	.07
LDL-C/HDL-C	Baseline	3.00 (0.94) (57)	3.12 (1.07) (57)	.53
	3 months	3.16 (0.94) (52)	2.80 (1.12) (51)	.07
	6 months	3.19 (1.01) (51)	2.66 (1.08) (50)	.01
	9 months	2.92 (0.88) (48)	2.70 (1.10) (50)	.28
	12 months	2.89 (0.80) (48)	2.77 (0.98) (48)	.51

Values are mean and standard deviation. Number of patients at each visit is given in parenthesis. The numbers vary because of drop-outs (**Figure 1**). Missing values were replaced by linear interpolation in SPSS. Comparisons between control and NS groups were done by independent sample t test. Statistically significant differences are bolded. TG: Triglycerides; TC: Total cholesterol; LDL-C: Low density lipoprotein cholesterol; HDL-C: High density lipoprotein cholesterol

Table 3. Comparison of body mass index, heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure at different treatment durations, between the control and *Nigella sativa* groups.

Variables (Mean ± SD)	Treatment duration	Control	<i>N sativa</i>	P value
BMI (kg/m ²)	Baseline	31.83 (3.93) (57)	30.47 (3.99) (57)	.071
	3 months	32.09 (3.76) (52)	30.68 (3.83) (51)	.064
	6 months	32.15 (3.88) (51)	30.76 (3.74) (50)	.071
	9 months	32.06 (4.11) (48)	30.69 (3.66) (50)	.085
	12 months	32.14 (4.12) (48)	30.84 (3.51) (48)	.101
HR (beats/minute)	Baseline	87.40 (8.83) (57)	85.80 (7.64) (57)	.305
	3 months	87.57 (7.73) (52)	84.09 (6.13) (51)	.013
	6 months	88.19 (7.65) (51)	84.04 (7.31) (50)	.006
	9 months	88.45 (9.17) (48)	84.28 (6.86) (50)	.013
	12 months	88.16 (7.76) (48)	82.68 (7.16) (48)	.001
SBP (mmHg)	Baseline	133.77 (14.37) (57)	139.03 (15.68) (57)	.053
	3 months	131.53 (14.70) (52)	133.92 (18.82) (51)	.475
	6 months	131.76 (13.25) (51)	132.90 (20.07) (50)	.738
	9 months	134.68 (14.34) (48)	132.00 (16.22) (50)	.388
	12 months	134.37 (15.32) (48)	129.37 (17.43) (48)	.139
DBP (mmHg)	Baseline	78.59 (7.60) (57)	80.17 (8.34) (57)	.293
	3 months	78.26 (5.41) (52)	76.27 (8.47) (51)	.157
	6 months	78.52 (7.02) (51)	76.10 (8.70) (50)	.126
	9 months	80.41 (7.13) (48)	77.20 (6.71) (50)	.024
	12 months	79.89 (7.88) (48)	76.66 (7.80) (48)	.47
MAP (mmHg)	Baseline	96.92 (7.89) (57)	99.75 (9.26) (57)	.083
	3 months	96.23 (7.59) (52)	95.31 (10.31) (51)	.607
	6 months	95.67 (7.91) (51)	95.11 (10.54) (50)	.607
	9 months	98.77 (8.37) (48)	95.69 (8.73) (50)	.078
	12 months	98.15 (9.43) (48)	94.01 (9.78) (48)	.038

Values are mean and standard deviation. Number of patients at each visit is given in parenthesis. Number of patients varies because of drop outs. Missing values replaced by linear interpolation in SPSS. Comparisons between control and NS groups were done by independent sample t test. Statistically significant differences are bolded. BMI: body mass index; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure.

tracts from *N sativa* on both HR and contractility of isolated guinea pig heart.³¹ In contrast, a rise in HR and cardiac contractility was induced in isolated perfused rat hearts treated with *N sativa*.³²

BMI in the present study did not differ significantly in either the placebo or *N sativa* groups when compared to their baseline values or to each other. In contrast to our result, a study in males with central obesity found a significant reduction in body weight and waist circumference with *N sativa*.¹⁹ Additionally, a nonsignificant reduction in abdominal circumference has been reported in patients

with insulin resistance syndrome treated with *N sativa* oil.³³ However, results reported by Le et al¹⁰ suggested that petroleum ether extract of *N sativa* caused a 25% reduction in food intake that translated into a transient weight loss in normal rats.

The relationship between dyslipidemia and hypertension has been well recognized.³⁴ Therefore, the prominent lipid lowering and antiatherogenic effects of *N sativa* demonstrated in the current study might, in part, play a role in reducing blood pressure. A study in Turkish hypertensive patients reported that poor BP con-

trol despite appropriate treatment was associated with metabolic syndrome, diabetes, and undertreatment of atherogenic dyslipidemia.³⁵ Tan et al indicated that prehypertension is associated with atherosclerosis, independent of conventional cardiovascular risk factors in type 2 diabetic patients, speculating that maintenance of SBP and DBP within a normal range may reduce the risk of atherosclerosis in type 2 diabetes.³⁶

The precise mechanism by which *N sativa* may induce its favorable potential on lipids and blood pressure is not fully elucidated. However, several lines of evidence are accumulating denoting a pivotal role for oxidative stress in the pathogenesis of dyslipidemia³⁷ and hypertension.³⁸ The beneficial effects of *N sativa* on lipid levels and blood pressure demonstrated in the current study may be explained by the high antioxidant potential of *N sativa*, reported previously.^{39,40}

Studies on TQ have shown a significant reduction in (elevated) lipid levels and improvement in (altered) levels of lipid peroxidation products as well as antioxidant enzymes. These data suggested a high antioxidant potential for TQ in rats with doxorubicin-induced nephropathy⁴¹ and for ethanol extract of *N sativa* seeds in streptozotocin-induced diabetic rats.⁴²

Basal superoxide anion production was reported to increase in spontaneously hypertensive rats, compared to normotensive rats.⁴³ Consequently, superoxide anion scavenging by the use of the TQ was shown to lower blood pressure in nitric oxide deficient hypertensive rats.⁴⁴ Recently, *N sativa* and its active constituents have exhibited antioxidant, hypotensive, calcium channel blockade and diuretic properties, which may contribute to reduced blood pressure, suggesting a potential role for *N sativa* in the management of hypertension.⁴⁵

Our study adds to the reliability of a growing number of studies that have contributed evidence on the beneficial effects of *N sativa* on serum lipids as reflected in a recent systematic review based upon 17 clinical trials.¹⁸

Now there is enough evidence from animal as well as human studies to test the use of *N sativa* in larger populations who have or who are at risk of lipid derangements.

Our study has quite a few limitations. We initially planned to include patients with elevated lipids and group them into three (namely placebo, statins and *N sativa*); however the clinicians on our team disagreed on the ground that it would be unethical to not give recognized treatment (statins) to diabetic patients with lipid derangements. Random allocation was not feasible due to limitation of informed consent and rigorous exclusion criteria. However, we feel that despite utmost care and observance of a well defined and restricted selection criteria there is possibility of allocation bias.

Patients were generally found the suggestion of a long follow up unappealing. Although sample size was calculated and the number of subjects inducted accordingly, there were subjects lost to follow up. Missing subjects were not necessarily the same in the subsequent follow ups as some of the subjects missed one follow up visit and reappeared at the next visit. This made adherence to sample size impossible. This would definitely reduce the significance of the results.

In conclusion, *N sativa* supplementation over a one-year period effectively reduced TC, MAP and HR in type 2 diabetic patients receiving OHA. This suggests that *N sativa* seeds might be useful as a complementary therapy with other antiatherogenic and antihypertensive drugs for the management of diabetic complications. This may open the field for a novel preventive therapeutic strategy tailored to reduce CVD in this large population at risk.

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Conflict of interest

Authors declare no conflict of interests.

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