

Blood Pressure and Lipid Lowering Effects of Nigella sativa Seeds and Honey Mixture

Sarina Mohamad,^{1,2} Nor Hayati Ibrahim,¹ & *Hayati Mohd Yusof¹

¹School of Food Science and Technology, Universiti Malaysia Terengganu, Malaysia. ²Universiti Teknologi MARA (Terengganu), Kuala Terengganu, Chendering 21080, Terengganu, Malaysia.

Abstract: The aim of this study was to investigate the effect(s) of a mixture of Nigella sativa seeds (*N. sativa*; black cumin or fennel) and honey on (i) the modulation of cardiovascular disease (CVD) risks among hypercholesterolemic and healthy subjects; and (ii) to assess the lipid-soluble antioxidants capacity of samples using the photochemiluminescence (PCL) method. Sixty-five subjects, aged twenty-five to fifty-eight, were enrolled and assigned to three groups. Two groups of healthy and hypercholesterolemic subjects were supplemented with *N. sativa* seeds and honey at 50 mg/kg (body weight) daily for three months. The third group served as control (healthy subjects without supplementation). Fasting blood samples were taken at baseline and again after three months of supplementation to measure (i) total cholesterol (TC), (ii) triglycerides (TG), (iii) low density lipoprotein-cholesterol (LDL-c), (iv) high density lipoprotein-cholesterol (HDL-c), (v) blood glucose, and (vi) hemoglobin concentrations. The findings were significant ($p < 0.05$), indicating that *N. sativa* seeds mixed with honey had hypolipidemic, antiobesity and hypotensive effects. Results showed significant reductions in TG (20.1%), TC:HDL-c (12.3%), accompanied by increased HDL-c (15.0%) among healthy subjects. Supplementation also significantly decreased TC (6.2%), TG (13.3%), TC:HDL-c (19.5%), with increased HDL-c (8.4%) in the hypercholesterolemic group. Furthermore, there were significant reductions in body weight, body mass index and body fat by 2.3%, 2.2%, 4.5%, and by 1.8%, 1.9%, 4.5% in healthy and hypercholesterolemic subjects, respectively. Blood pressures lowering were also observed in hypercholesterolemic subjects with significant reductions in systolic blood pressure (3.9%) and diastolic blood pressure (5.5%). There were no significant effects from supplementation on blood glucose or hemoglobin concentrations. It is postulated that the positive effects observed may be due to antioxidant activity. The combination of *N. sativa* seeds with honey showed higher synergistic effects when compared with supplementation of *N. sativa* seeds or honey on their own. Overall, these findings suggest that a mixture of *N. sativa* seeds with honey has beneficial effects in lowering the cited risk indicators for cardiovascular disease as a natural source of antioxidant activity; thus aiding the maintenance of health by lowering CVD risk factors.

Keywords: lipid profile, antihypertensive, antiobesity, *N. sativa* seeds, honey, antioxidant activity

I. Introduction

CVD is an endemic and chronic human disease that over the past century has remained a common public health problem globally (Caterina et al. 2006). According to the World Health Organization (WHO, 2008), it is estimated that 17.1 million people died from CVD in 2004 and that this rate will increase to 23.4 million by 2030. Hence, CVD remains a leading cause of death in both developed and developing countries (Chia, 2011; WHO, 2011). By 2020 it is expected to be the main cause of morbidity and mortality in most developing countries (Celermajer et al. 2012). In Malaysia, CVD incidence has increased rapidly in recent years (National Cardiovascular Disease, 2007), and is responsible for 17% of deaths in government hospitals nationwide (National Heart Association, 2011).

The use of natural supplements for disease management is both commonly practiced and gaining more attention. However, until now, there is a dearth of systematically and scientifically ordered studies on the efficacy of dietary supplementation. The present study was initiated based on indications in Sura An-Nahl (The Bees), verse 69:

“... There comes forth from their bellies a drink of varying hues. Therein is a cure for men. Surely, in that is a Sign for people who reflect.”

There is also a supporting hadith narrated by Ibnu Majah, where the Prophet Muhammad (Peace Be Upon Him) said;

“Hold on to the use of the black seed, for it has the cure for every illness except death” (Mawsu’ah al-Hadith al-Syarif al-Kutub al-Sittah).

Previous studies have been carried out on the utilization of *N. sativa* seeds and honey because of empirically known beneficial impacts which include CVD risk factors. The seeds of *N. sativa* contain both fixed and volatile oils (Salem, 2005; Cheikh-Rouhou et al. 2007; Sultan et al. 2009). They are also rich sources of unsaturated fatty acids and quinones, especially thymoquinone (Butt & Sultan, 2010; Lutterodt et al. 2010). *N.*

sativa seeds have also been shown to improve blood lipid profiles in human studies (Bhatti et al. 2009; Tasawar et al. 2011; Mahmood et al. 2012; Sabzghabae et al. 2012). Human studies on the therapeutic effects of *N. sativa* seeds have also revealed hypoglycemic effects (Bamosa et al. 2010; Mohtashami et al. 2011); as well as hypotensive effects (Dehkordi & Kamkhah, 2008); hematologic effects (Bamosa et al. 2010; Mohtashami et al. 2011); and antiobesity effects (Haque et al. 2011; Ghurbakhshani et al. 2012).

Similarly, other human studies have reported that honey possesses beneficial effects on CVD risk factors and the blood lipid profile (Yaghoobi et al. 2008; Mushtaq et al. 2011); as well as on hemoglobin concentration (Al-Waili et al. 2006); and on body weight (Yaghoobi et al. 2008). However, up to the present, studies of honey's effects on blood glucose levels have been limited to animal trials (Fasanmade & Alabi, 2008; Sheriff et al. 2011); and on blood pressure (Oztasan & Songur, 2007; Erejuwa et al. 2012).

In most studies, favourable effects derived from *N. sativa* seeds and honey have been reported separately. Only two studies have been done on their mixture and these were limited to healthy subjects. Moreover, the effectiveness of any intervention is more pronounced in secondary prevention settings (e.g., patients with high lipid profiles). No research has been attempted on the effects of a mixture of *N. sativa* seeds and honey in hypercholesterolemic subjects as a secondary intervention. Therefore, it was anticipated that the present study would provide robust evidence in support of *N. sativa* seeds and honey in combination as a health supplement. Additionally, the present study is significant as it is the first to investigate the effects of *N. sativa* seeds and honey in modulating risk factors for CVD as both primary and secondary measures.

II. Materials and Methods

Subjects Selection

Sixty five male and female subjects were enrolled in this study. All subjects were provided with full disclosure via a subject information sheet. Inclusion criteria for healthy subjects were as follows; twenty-five to fifty-eight years of age and no chronic diseases such as hypothyroidism, diabetes mellitus, gastrointestinal disorders, renal impairment or cardiac problems, not taking medications (lipid-lowering drugs, anti-diabetic, aspirin), not taking any dietary supplements, not vegetarian, not a vigorous exerciser (no more than three thirty minute vigorous sessions per week), not pregnant or lactating, not a heavy smoker (< 10 cigarettes per day), not a blood donor for at least three months, not planning to lose weight, not participating in any clinical trial for the last three months. The sample size for this study was determined by using Altman's Normogram with the assumption that the effective size was 1.1 and the experiment had a test power of 98%. This study was approved by the Universiti Malaysia Terengganu Committee of Research following the university's ethical standards for human trials.

Study Design

The study was conducted from May 2012 through October 2012. All eligible subjects provided a written informed consent form prior to initiating the trial, and each participant was screened by a Health and Lifestyle Questionnaire. Baseline data for all participants was taken at the first visit. Subjects were categorized into three groups: (1) a control group of healthy subjects without supplementation (n= 20); (2) a group of healthy subjects supplemented with a paste mixture of *N. sativa* seeds and honey (n=22); and (3) a hypercholesterolemic supplementation group at CVD risk (hypercholesterolemia, n=23), all of whom were supplemented with the paste mixture of *N. sativa* seeds and honey. Subjects were required to consume the supplement daily according to the dosage as instructed for three months (50 mg/kg of body weight). No placebo was used for the control group because it was too difficult to mimic the unique taste and aroma of the paste. During the supplemental period, subjects were advised to maintain their usual daily lifestyles. Each participant was followed-up monthly to remind them to consistently consume the paste as instructed.

Data Collection and Measurements

Height was measured using a portable stadiometer (SECA, Germany) and results were recorded to the nearest 0.5 cm. Body weight was determined by using the Tanita digital body fat monitor/scale model: UM-026 (Tanita, UK), recorded to the nearest 0.1 kg. Body fat percentage was determined by using the Tanita digital body fat monitor/scale, model UM-026 (Tanita, UK), recorded to the nearest 0.1%. Systolic blood pressure was measured from the left arm using an Omron Automatic Blood Pressure Monitor, HEM-7080, following the NICE Guideline (2011).

Blood collection was carried out in the morning after an overnight fasting of at least 10 hours. 40 µL of whole blood was collected using a capillary blood collector to determine total cholesterol (TC), triglycerides (TG), high density lipoprotein-cholesterol (HDL-c), and low density lipoprotein-cholesterol (LDL-c) using Lipid Panel Test Strips with the auto CardioChek P•A™ Analyzer (Polymer Technology System, USA). Classification of the blood fasting lipid profile was based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP, 2001). Fasting blood glucose level was determined by glucose reagent test strip with

the Accu-Check Advantage Meter (Roche Diagnostics, Germany). Hemoglobin concentration was determined by using the HemoCue[®] B-Hemoglobin microcuvettes and HemoCue B-Hemoglobin Photometer (HemoCue AB, Sweden).

The final data was collected during the second visit during which subjects were required to return the remaining paste mixture, which was then weighed as a measure of compliance. Subjects who consumed less than 90% of the provided supplement were excluded from the final analysis. Of the sixty-five subjects recruited, data from sixty-one was used for the final analysis. A summary of study design is shown in Figure 1.

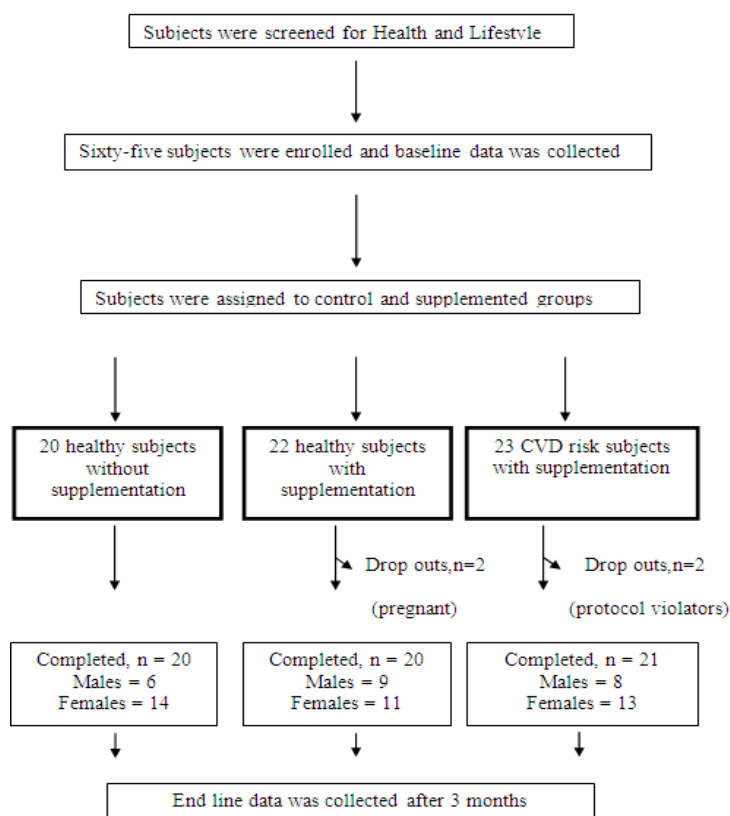


Figure 1: Study Design

The antioxidant capacity of lipid-soluble substances was assayed by luminol-photochemiluminescence according to the procedure used by Popov and Lewin (1999) as adapted to standard ACL protocol. Lipophilic antioxidants were measured with the Photochem[®] instrument (Analytik Jena AG, Jena, Germany) using the antioxidant capacity, lipid-soluble substance (ACL) kit.

All data were statistically analyzed with SPSS software, version-18 (SPSS Inc., Chicago, IL). A paired sample t-test and variance analytics (one-way ANOVA) were applied. For variables where the criterion for normality was not met, corresponding non-parametric tests, as per the Wilcoxon Signed Rank and Kruskal-Wallis tests, were utilized (Pallant, 2011). Data was presented with a mean (SD) or median (10th, 90th percentile). In all cases, the ‘P’ value ≤ 0.05 was taken to indicate a significant effect.

III. Results and Discussion

Table 1 shows the baseline characteristics of the subjects according to groups. Based on the amount of returned *N. sativa* seeds and honey paste for the supplemented groups, compliance was high, at 98.8%. In addition, no adverse effects were reported by participants. Table 2 shows the effects of supplementation on the lipid profiles. These results represent the first reported effects of *N. sativa* seeds mixed with honey as a supplement for hypercholesterolemic subjects. Previous studies reported the effects of *N. sativa* seeds mixed with honey on lipid profiles observed in healthy subjects only (Yusof et al. 2012). Table 2 also shows changes in lipid profiles for all three groups at the end of the study’s intervention.

Table 1: Baseline Characteristic of the Participants

Parameter	Group			F-statistics (df) or χ^2 -statistics (df)	P-value
	Control (n=20)	Healthy supplementation (n=20)	Hypercholesterolemic supplementation (n=21)		
Age (year)	34.5 (8.9)	38.5 (8.1)	37.9 (9.4)	1.2 (2, 58)	0.317
Systolic Blood Pressure (mmHg)	117.1 (14.2)	119.9 (17.1)	123.8 (21.6)	0.721 (2, 58)	0.490
Diastolic Blood Pressure (mmHg)	79.2 (12.7)	81.7 (11.4)	85.1 (14.0)	1.139 (2, 58)	0.327
Body Weight (kg)	63.7 (14.8)	75.1 (18.3)	70.3 (15.4)	2.478 (2, 58)	0.093
Body Mass Index (kg/m ²)	25.5 (20.3, 30.4)	27.6 (21.6, 38.5)	26.2 (22.9, 36.3)	3.447 (2, 61)	0.178
Body Fat (%)	27.3 (8.3)	29.2 (7.9)	29.2 (7.8)	0.358 (2, 58)	0.700
Hemoglobin Concentration (g/dL)	14.6 (1.5)	14.3 (1.5)	14.4 (1.6)	0.183 (2, 58)	0.833
Fasting Blood Glucose (mmol/L)	5.4 (0.4)	6.0 (0.7)	6.0 (0.7)	5.518 (2, 58)	0.006 ^e
Total Cholesterol (mmol/L)	4.49 (0.57)	4.69 (0.36)	6.17 (1.06)	32.801 (2, 58)	0.000 ^e
HDL-c (mmol/L)	1.48 (0.44)	1.25 (0.36)	1.54 (0.45)	2.760 (2, 58)	0.072
LDL-c (mmol/L)	2.57 (0.61)	2.76 (0.41)	4.02 (0.97)	25.607 (2, 58)	0.000 ^e
Triglycerides (mmol/L)	0.88 (0.58, 1.38)	1.35 (0.63, 2.63)	1.09 (0.62, 3.53)	6.016 (2, 61)	0.049
Ratio TC:HDL-c	3.3 (1.10)	4.1 (1.18)	4.3 (1.15)	4.123 (2, 58)	0.021 ^e

Data are presented in mean (SD) or median (10th, 90th percentile)

^e p < 0.05 indicate significant difference by One-way ANOVA Test

p < 0.05 indicate significant difference by Kruskal-Wallis Test

The present study found that the *N. sativa* seeds and honey mixture had pronounced effects on blood lipid profiles with significant overall reductions in TG by twenty percent and with significant elevations in HDL-c by fifteen percent in healthy supplemented subjects. Of greater significance was the supplement's beneficial effect on the hypercholesterolemic group with an overall reduction of TC by 6% and TG by 13.3%; also reduced LDL-c by 6.7% (but not statistically significant), with a significant increase in HDL-c by 8.4% (p < 0.05) (Table 2). Lipid lowering for both supplemented groups is possibly due to the effect of nigellamines contained in *N. sativa* seeds (Tulukcu, 2011). In addition, it has been reported that fructooligosaccharides (FOS) in honey inhibit fatty acid synthesis in the liver, resulting in TG reduction (Nemoseck et al. 2011).

Table 2: Effects of Supplementation on Blood lipid and Blood Pressure

Parameter/Trial Group	Control (n=20)	Healthy supplementation (n=20)	Hypercholesterolemic supplementation (n=21)
Total Cholesterol (mmol/L)			
Baseline	4.49 (0.57)	4.69 (0.36)	6.17 (1.06)
Endline	4.77 (0.71)	4.66 (0.58)	5.73 (0.71)
Percent change (%)	6.9 ^a	-0.04 ^{ab}	-6.2 ^b
HDL-c (mmol/L)			
Baseline	1.48 (0.44)	1.25 (0.36)	1.54 (0.45)
Endline	1.50 ^a (0.42)	1.41 ^b (0.37)	1.79 ^b (0.38)
Percent change (%)	-2.5 ^a	15.0 ^b	8.4 ^b
LDL-c (mmol/L)			
Baseline	2.57 (0.61)	2.76 (0.41)	4.02 (0.97)
Endline	2.85 (0.77)	2.87 (0.44)	3.66 (0.68)
Percent change (%)	12.4 ^a	4.7 ^{ab}	-6.7 ^b
Triglycerides (mmol/L)			
Baseline	0.88 (0.58, 1.38)	1.35 (0.63, 2.63)	1.09 (0.62, 3.53)
Endline	0.85 (0.58, 1.67)	0.99 (0.55, 1.96)	0.79 (0.55, 1.69)
Percent change (%)	-7.5	-20.1	-13.3
Ratio TC: HDL-c			
Baseline	3.00 (2.01, 5.14)	3.86 (1.49)	4.10 (2.90, 5.98)
Endline	3.25 (2.20, 5.39)	3.50 (0.77)	3.10 (2.62, 5.26)
Percent change (%)	4.4 ^a	-12.3 ^b	-19.5 ^b
Systolic Blood Pressure (mmHg)			
Baseline			

Endline	117.1 (14.24)	119.9 (17.12)	123.8 (21.62)
Percent change (%)	115.9 (14.32)	114.7 (13.91)	□118.0 (17.45)
	-0.9	-2.3	-3.9
Diastolic Blood Pressure (mmHg)			
Baseline			
Endline	79.2 (12.68)	81.7 (11.44)	85.1 (14.03)
Percent change (%)	76.5 (11.90)	78.3 (9.60)	□79.9 (12.09)
	-2.9	-1.2	-5.5

Data are presented in mean (SD) or median (10th, 90th percentile) □ or □□ indicate significant difference between baseline and endline in a column by Paired t-Test or Wilcoxon Signed Rank Test

Values with different superscript letter indicates significant difference by One-way ANOVA or

However the hypolipidemic effect of a mixture of *N. sativa* seeds and honey on cholesterol lowering activity are not fully understood. It is postulated that the effect is due to synergistic activity of the supplement's different constituents. In *N. sativa* seeds, the pharmacological actions of active constituents such as thymoquinone (TQ), sterols, flavonoids, soluble fiber and polyunsaturated fatty acids (PUFAs) (Butt & Sultan, 2010; Lutterodt et al. 2010) have demonstrated important roles in the reduction of plasma cholesterol. Moreover, the antioxidant components of *N. sativa* seeds (fixed and essential oils) may inhibit lipid peroxidation (Sultan et al. 2009). Since the exact pathways of such activities are not yet well defined, the lipid-lowering activity of *N. sativa* seed might be due to a modulation of HMG-CoA reductase activity, as well as increased levels of LDL-receptors and the prevention of LDL-oxidation through antioxidant mechanisms (Ahmad & Beg, 2013). It is also possible to reduce cholesterol levels through intestinal cholesterol absorption which is inhibited by plant sterols (Trautwein et al., 2003).

Honey has also demonstrated lipid-lowering activities that are likely due to antioxidant effects on lipid metabolism (Nemoseck et al., 2011). In addition, honey was reported to have favorable effects on lowering TC and LDL-c while enhancing HDL-c levels (Chepulis & Starkey, 2008). The antioxidant activity of honey has also been suggested as a beneficial adjunct influencing lipid metabolism (Nemoseck et al. 2011). Al-Waili (2004) observed the effects of 75 g of natural honey on hyperlipidemic patients for fifteen days and found that honey significantly reduced TC by eight percent and LDL-c by eleven percent. Yaghoobi et al. (2008) also found that honey reduced TC by 3.3%, TG by 19%, LDL-c by 4.3%, while enhancing HDL-c production in obese patients after a month of supplemental treatment with 70 g of natural honey daily. These results are in accordance with Mushtaq et al. (2011), whose group obtained similar results (reduction of TC, TG, and LDL-c with increased HDL-c) in obese subjects after a month of supplementation with 40 g of honey dissolved in water with regular meals. To the contrary, Hussain et al. (2012) reported no significant effect in the lipid profile among healthy postmenopausal Malay women after four months of supplementation with Tualang honey at 20 g/day.

In terms of blood glucose and hemoglobin levels, results demonstrated no significant observable changes consistent with previous studies which reported that neither *N. sativa* seed/extract nor honey had any significant effects on either blood glucose levels (Sabzghabae et al. 2012; Hussain et al. 2012), or hemoglobin concentrations. Thus, the present results did not exhibit hypoglycemic effects for *N. sativa* seed and honey mixture. This might be due to the fact that participants were not glucose intolerant or diabetic patients.

The present study demonstrated that the *N. sativa* seeds and honey mixture had a hypotensive effect in the hypercholesterolemic supplementation group but did not significantly affect blood pressure in healthy subjects (Table 2). The insignificant reduction of blood pressure in normotensive subjects of the healthy supplementation group agrees with Yusof et al. (2012) who also studied the effects of *N. sativa* seeds and honey mixture on the blood pressure of healthy individuals. No other studies of the effect of honey on blood pressure in humans has been previously reported.

Table 3 indicates that body weight and BMI increased and body fat was slightly decreased in the control group when compared to baseline values, but were statistically not significant ($p > 0.05$). The antiobesity effect of the *N. sativa* seed and honey mixture might be due to various components in the *N. sativa* seed, especially lipase which is responsible for antiobesity activity (Haque et al., 2011), but the exact mode of activity is not yet fully understood (Shah et al., 2012). Possible explanations include the antioxidant activity of honey or its lower glycemic index in the regulation of body weight (Nemoseck et al., 2011). Nemoseck et al. (2011) reported that honey may have the potential to suppress appetite which causes a reduction in food intake by increasing the production of serum leptin levels.

Table 3: Body Weight, BMI and Body Fat at Baseline and After Three Months Supplementation

Parameter/Trial Group	Control (n=20)	Healthy supplementation (n=20)	Hypercholesterolemic supplementation (n=21)
Body Weight (kg)			
Baseline	63.7 (14.80)	75.0 (18.31)	70.2 (15.35)
Endline	64.0 (15.64)	□72.1 (17.58)	□68.9 (15.18)
Percent change (%)	0.17	- 2.26	- 1.83
Body Mass Index (kg/m ²)			

Baseline	25.0 (4.64)	27.6(21.6, 38.5)	26.2 (22.9, 36.3)
Endline	25.1 (4.86)	□26.4(21.1, 37.2)	□25.6 (23.1, 35.5)
Percent change (%)	0.18	- 2.24	- 1.92
Body Fat (%)			
Baseline	27.32 (8.26)	29.2 (7.88)	29.2 (7.82)
Endline	27.27 (7.77)	□27.7 (7.36)	□27.7 (8.20)
Percent change (%)	1.03	- 4.46	- 4.50

Data are presented in mean (SD) or median (10th, 90th percentile)

□ or □ indicate significant difference between baseline and endline in a column by Paired t-Test or Wilcoxon Signed Rank Test

The findings of the current study are also consistent with Yusof et al. (2012) whose group found that *N. sativa* seeds and honey mixture produced an antiobesity effect. Results from this study showed greater weight loss (reduced body weight, BMI and body fat by 2.3%, 2.2% and 4.5%, respectively in healthy subjects; and by 1.8%, 1.9% and 4.5%, respectively in hypercholesterolemic subjects). It is possible that these results are due to the longer duration of the study and its larger sample size.

Figure 2 indicates that the lipophilic antioxidant capacity of honey, *N. sativa* seeds, and a mixture of *N. sativa* seeds and honey as Trolox equivalents were 7.18 (0.28), 9.67 (0.19) and 29.94 (0.75) µg/mg, respectively. Interestingly, these results indicate that the mixture of *N. sativa* seeds and honey demonstrated the highest antioxidant capacity. This finding suggests that lipid-soluble antioxidants in whole seeds of *N. sativa* have a synergistic effect when combined with antioxidants available in honey, thus causing a higher antioxidant capacity for the mixture as compared to either *N. sativa* seeds or honey alone. This result further suggests that consumption of the *N. sativa* seeds and honey mixture at lower dosage (50 mg/kg body weight), when compared to previous studies, exhibited positive effects on the modification of the lipid profile and CVD risk factors. Based on previous studies, consumption of *N. sativa* seeds or honey alone required higher dosages: 2 – 18.4 g/day of *N. sativa* seeds (Sabzghabae et al. 2012; Ghurbakhshani et al. 2012) and 40 – 80 g/day of honey (Al-Waili, 2004; Al-Waili et al. 2006; Mushtaq et al. 2011) in order to improve the lipid profile.

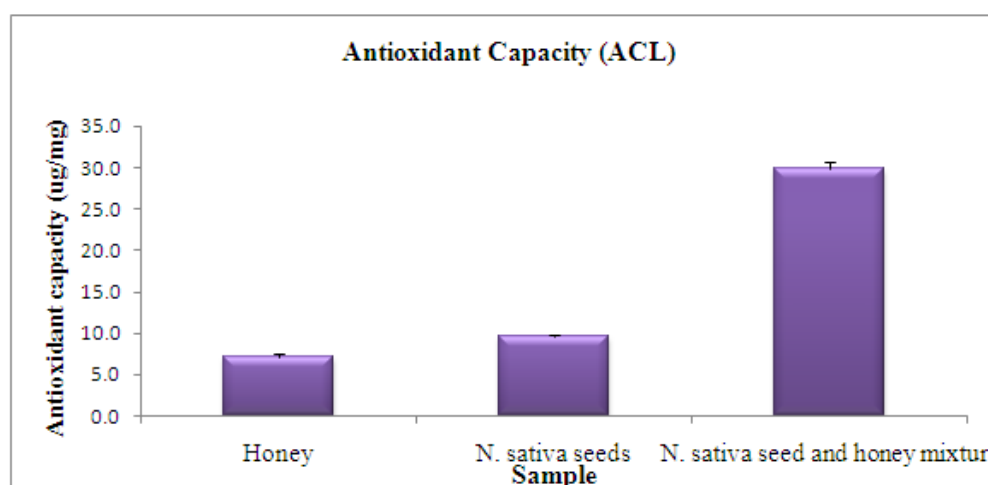


Figure 2: Lipid-soluble antioxidant capacity [Trolox equivalent (µg/mg)] of *N. sativa* seeds, honey and mixture of *N. sativa* seeds and honey assayed by photochemiluminescence (PCL-ACL)

A possible explanation for this result might be related to major bioactive constituents in the seeds of *N. sativa* as fat-soluble antioxidant compounds (Salem, 2005; Cheikh-Rouhou et al. 2007; Sultan et al. 2009), with the assumption that it is rich in thymoquinone (TQ) as an oil extract (Butt & Sultan, 2010; Lutterodt et al., 2010). TQ has been shown to exert an antioxidative effect (Ashraf et al. 2011) through inhibiting the generation of the superoxide anion radical (O₂^{•-}) (Mezeti et al. 2012). In addition, the natural antioxidant phenolics in honey can be classified into lipophilic or hydrophilic groups that probably contributed to antioxidative activity via the reduction of lipid peroxidation (D'Arcy, 2005). Thus, it can be suggested that the variability of lipid-soluble antioxidant components in the *N. sativa* seeds and honey mixture may have directly modulated lipid profiles for subjects in this study. Lipid-soluble antioxidant compounds have been reported to have the capability to neutralize free radicals cell membrane fats by inhibiting lipid peroxidation (Gupta & Sharma, 2006). Hence, oxidation of LDL-c, by which the oxidized LDL-c both accumulates and is deposited on arterial walls, subsequently leading to cardiovascular disease, can be avoided (Yashin et al., 2010).

Over recent decades, studies have successfully focused on determining both the general and specific antioxidant activities of various extracts (Mohamed et al. 2010; Mezeti et al. 2012). Until now, no report has

surfaced on the lipid-soluble antioxidant capacity of crude *N. sativa* seeds, of honey, or of the mixture of *N. sativa* seeds and honey. Thus, the current finding of the lipid-soluble antioxidant capacity of *N. sativa* seeds, of honey, and of a mixture of *N. sativa* seeds and honey have been revealed for the first time by photoluminescence (PCL-ACL) assay. The overall findings of the present study demonstrated that a mixture of *N. sativa* seeds and honey has beneficial effects, not only as a nutritious health supplement, but also as a natural source of antioxidants for maintenance of health by preventing or lowering risks for cardiovascular disease.

IV. Conclusion

The present results demonstrate significant cardioprotective effects based on lipid profile modulation among hypercholesterolemic subjects when compared to healthy subjects. This clearly suggests that the *N. sativa* seeds and honey mixture has a positive effect on the management of CVD. This key finding calls for further research in which different dosages of the *N. sativa* seeds and honey mixture may be utilized in order to identify optimal dosages for more effective and efficient lowering of the lipid profile in order to help reduce CVD morbidity and mortality.

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