In vivo Antioxidant-Related Effect of Orally Administered Ground Seeds of *Nigella sativa* in Human Volunteers

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ABSTRACT

Nigella sativum which belongs to the family Ranunculaceae, is one of the important medicinal plant species. The present study aimed to assess antioxidant- related effects of *Nigella sativum* in human volunteers and its effects on liver, renal and cardiac function tests. 9 healthy volunteers participated in the study and each received 1 spoon from ground seeds of *Nigella sativum* daily for five days. Blood samples were taken before and 1 hour after the administration of 1 spoon from ground seeds of *Nigella sativum* (samples 1 and 2, respectively) and then one day after the last dose of day five (sample 3). The first blood taken before the first dose (sample 1), served as the control for the next samples (2 & 3). Serum total antioxidant status (TAS), erythrocyte reduced glutathione (GSH), malonyldialdehyde (MDA), and serum selected biochemical tests were used as assays. Oral administration of ground seeds of *Nigella sativum* to healthy volunteers, for five days increased the serum TAS and serum erythrocyte GSH significantly, with no impact on serum biochemical tests for kidney, liver, cardiac and pancreatic parameters. In conclusion, as the current outcomes are based on healthy humans with no oxidative stress, this shows that oral administration of ground seeds of *Nigella sativum* can improve the baseline of the defense mechanisms against possible oxidative stress, with no adverse effects, thus decreasing susceptibility or preventing the progress of pathological conditions related to oxidative stress.

Key Words: *Nigella sativum, Total Antioxidant Status, MDA, GSH, Superoxide Dismutase, Serum Biochemical Tests, in Vivo.*

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INTRODUCTION

Nigella sativa (*N. sativa*) (Family Ranunculaceae) is a medicinal plant that is grown almost all over the world. [1] *N. sativa* has several different common names depending on the country such as black seed, black cumin, black caraway, "kalonji" (in India), "Kalo jeera" (in Bangladesh), "Hak Jung Chou" (in China), and 'Habbah Sawda' or "Habbat al-barakah" (in the Middle East). [2, 3]

Recent reports demonstrated antihypertensive, diuretic, antidiabetic, immunomodulatory, antimicrobial, anticancer, anthelmintics, anti-inflammatory analgesics, spasmolytic, bronchodilator, gastroprotective, hepatoprotective, renal protective and antioxidant properties potential of *N. sativa*. [4-12].

Free radicals are continuously produced in the human body. These oxygen species are the cause of cell damage and the initiation and progression of chronic diseases. Therefore, there are lines of defense to protect body systems from oxidative injury that includes intracellular antioxidants such as reduced glutathione (GSH), superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione reductase (GR), glutathione S-transferase (GST) and catalase, and extracellular antioxidants such as vitamins, micronutrients, carotenoids, polyphenolics and other bioactive compounds [11, 12]

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The present study focused on the antioxidant-related effects of ground seeds of *Nigella sativum* on normal human volunteers after oral administration of ground seeds of *Nigella sativum f*or five days and the effects of oral administration of ground seeds of *Nigella sativum* for five days on liver, renal and cardiac function tests.

MATERIALS AND METHODS

Nine healthy volunteers (1 man and eight women) with a mean age of 36.7±14.1 years were recruited in the study after signing an informed consent according to the ethics committee requirements. Every volunteer received 1 spoon of ground seeds of *Nigella sativum* for five days. Blood samples were taken before and 1 hour after the administration of 1 spoon from ground seeds of *Nigella sativum* (samples 1 and 2, respectively) and then one day after the last dose of day five (sample 3). The first blood taken before the first dose (sample 1), served as the control for the next samples (2 & 3). This study was approved by the committee of the University of Jordan, and was performed in accordance with the moral standards ordered down within the 1964 declaration of Helsinki.

Blood Samples

Three blood samples were collected in gel clot activator tubes from every healthy volunteer. Sample 1 was collected before administration of 1 spoon of ground seeds of *Nigella sativum*, and sample 2 after 1 hour of the first dose (1 spoon from ground seeds of *Nigella sativum*) on day one and sample 3 at day 6 (i.e. one day following the last dose of day five). Gel tubes were centrifuged for ten min at 3000 xg at room temperature to separate and collect serum. Then 2 milliliters of distilled water was added to the cells under the gel in tubes and the tubes were centrifuged for five min at 3000 xg and therefore the supernatant (hemolysate) was collected. All samples (serum and hemolysate) were kept frozen at - 20°C till analysis.

Determination of serum TAS

Serum total antioxidant status was measured by TAS kit from Randox. The results were expressed as mmol/L.

Determination of Erythrocyte MDA

Stocks and Dormandy's method (1971) and thiobarbituric acid (TBA) modified by Srour et al. (2000) were used to determine Erythrocyte MDas a measure of lipid peroxidation [13]. All MDA concentrations were expressed as nmol/gHb.

Determination of Erythrocyte GSH

Erythrocyte GSH was determined using Ellman's method [14] with slight modification as described elsewhere. [15] All GSH concentrations were expressed in mg/g Hb.

Determination of Erythrocyte Superoxide Dismutas (SOD) Activity

Erythrocyte superoxide dismutas (SOD) was measured using kit from Randox. [16] The results were expressed as U/gHb.

Determination of Serum Biochemical Parameters

The kits for determination of serum biochemical parameters were purchased commercially from Roche and 902 Hitachi analyzer used to perform the parameters including potassium (K), serum sodium (Na), creatinine (CREA), urea nitrogen (BUN), albumin (ALB), uric acid (UA),), lactate dehydrogenase (LDH), total protein (TP), alanine transaminase (ALT), alkaline phosphatase (ALP), aspartate transaminase (AST), amylase (AMYL), and creatinine phosphokinase (CPK).

Statistical Analysis:

All data are reported as the mean ± S.D. The statistical analysis was performed using SPSS statistics 17. The results were compared by paired *t*-test. The results with a value of $P \leq 0.05$ were considered significant.

RESULTS:

The results of the in vivo study are shown in Table 1. As shown in this table, oral administration of 1 spoon of ground seeds of *Nigella sativum* to healthy volunteers for five days raised significantly the serum TAS (from 0.89 to 1.16) and erythrocyte GSH (from 0.67 to 0.87) compared to zero time administration. Oral administration of 1 spoon of ground seeds of Nigella sativum to healthy volunteers for five days had no significant impact on any of the subsequent serum parameters that remained among the reference ranges (sodium, potassium, urea nitrogen, creatinine, uric acid, albumin, total protein, alkaline phosphatase, lactate dehydrogenase, alanine transaminase, aspartate transaminase, creatinine phosphokinase, amylase that are measured at zero time, 1 hour once the primary dose of day 1, or at day 6 (i.e. one day following the last dose of day five) (Table 1).

Table 1. The results of the in vivo study of oral administration of ground seeds of *Nigella sativum* to healthy volunteers for 5 days to healthy volunteers. Each value represents the mean value ± S.D., (n =9), *P value ≤ 0.05, compared to 0 time administration. NM indicates not measured.

Measured parameter	Sample 1	Sample 2	Sample 3
Serum TAS (mmol/L)	0.89±0.2	1.1±0.25*	1.16±0.13*

Erythrocyte GSH (mg/gHb)	0.67±0.07	NM	0.87±0.08*
Erythrocyte SOD (U/gHb)	1103.0±72.0	NM	1224.1±179.7
Erythrocyte MDA(nmol/gHb)	14.1±0.7	NM	13.2±1.5
Serum K (ref value=3.7-5.2 mmol/L)	3.98±0.27	4.15±0.31	4.67±0.48*
Serum Na (ref value=135-145mmol/L)	144.7±1.7	144.1±1.9	144.2±2.8
Serum BUN (ref value=6-20 mg/dL)	11.7±2.8	11.8±2.8	11.0±2.0
Serum CREA(ref value= 0.6-1.3 mg/dL)	0.63±0.11	0.63±0.10	0.65±0.10
Serum UA (ref value= 3.5-7.2 mg/dL)	4.55±1.3	4.55±1.3	4.6±1.2
Serum ALB(ref value= 34-54 g/L)	44.5±2.7	43.5±2.5	48.1±3.6*
Serum TP (ref value = 60-85 g/L)	77.2±4.5	76.3±4.0	83.8±2.9*
Serum ALP(ref value=55-142 U/L)	84.4±59.8	83.7±55.0	89.6±64.7*
Serum AST (ref value= 8-40 U/L)	22.6±4.5	22.0±4.5	22.4±6.8
Serum ALT (ref value= 7-55 U/L)	22.0±8.0	21.7±8.1	21.1±7.8
Serum CPK(ref value=38-176 U/L)	103.5±23.2	106.5±25.5	115.7±65.4
SerumLDH(refvalue=200-450 U/L)	366.9±61.15	343.9±57.5	352.1±52.2
Serum AMY(refvalue=40-140 U/L)	60.0±21.8	59.9±21.5	67.0±22.6*

DISCUSSION

The present in vivo study on humans showed that oral administration for 5 days of ground seeds of *Nigella sativum* to healthy volunteers increased significantly the Serum TAS and serum erythrocyte reduced glutathione (GSH). As the present findings are obtained in healthy humans with no oxidative stress induction, this indicates that seeds of *Nigella sativum* can improve the baseline of the defense mechanisms against possible oxidative stress, thus decreasing susceptibility to diseases related to oxidative stress.

Absence of the effect of oral administration of ground seeds of *Nigella sativum* to healthy volunteers for 5 days on serum biochemical tests that remained within the reference ranges for kidney function (BUN,CREA), liver function enzymes and tests (ALT, AST, ALP, albumin, total protein), cardiac enzymes (CPK) and pancreatic amylase, indicates the absence of adverse effects on these organs. This result agrees with the findings. [15, 17-19]

However, the importance of the present in vivo study on healthy humans is also related to the lifestyle factors such as diet, physical activity, alcohol consumption, cigarette smoking and others that have been suggested to seriously influence the oxidative stress response in humans, tipping the balance of oxidative burden/antioxidant response to one side or the other. Accordingly, a diet rich in vegetables and natural antioxidants, favoring the antioxidant side, has been found to be preferred by long-lived healthy individuals. [20, 21]

CONCLUSION

As the present findings are obtained in healthy humans with no oxidative stress, this indicates that oral administration of ground seeds of *Nigella sativum* can improve the baseline of the defense mechanisms against possible oxidative stress, with no adverse effects, thus decreasing susceptibility or preventing the progress of pathological conditions related to oxidative stress.

Authors' contributions

NA designed the study and performed data collection, processing, and analysis. NA wrote and approved the final version of the manuscript.

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