

**International Journal of Biomedical and Advance Research**

ISSN: 2229-3809 (Online); 2455-0558 (Print)

Journal DOI: <https://doi.org/10.7439/ijbar>

CODEN: IJBABN

Original Research Article

***Nigella Sativa* a Promising Drug in Treatment of Diabetes and Prevention of Its Complication****Malak Al-Faki Ahmed<sup>1</sup>, Hassan Suleiman Mohammed<sup>2</sup>, Nahid Mahmoud Hassan Elamin<sup>3</sup> and Omer Abdel Aziz Musa<sup>4</sup>**<sup>1</sup>Department of Physiology, Faculty of Medicine, Nile valley university, Atbara, Sudan<sup>2</sup>Department of Pediatrics, Atbara Hospital, Ministry Of Health, Atbara, Sudan<sup>3</sup>Department of Maxillofacial and Diagnostic Science, College of Dentistry, Jazan University, Jazan, Saudi Arabia<sup>4</sup>Department of Physiology, Faculty of Medicine, Ribatt University, Khartoum, Sudan**Abstract**

**Introduction:** *Nigella sativa* (NS) - an annual herb belongs to the family Ranunculaceae- has been used as a remedy for many diseases. Many researches revealed its medicinal properties including antidiabetic, antioxidant and antidyslipidemic activities with a large margin of safety. Diabetes mellitus has high morbidity and mortality. Rapidly increasing pervasiveness worldwide needs to be encountered by increase in research to help lessen pervasiveness as well as reduce its complications.

**Aim:** This study was conducted to validate hypoglycemic effect of NS on type 1 diabetic patients and safety of the seeds.

**Methodology:** 25 diabetic patients of both gender aged 5-17 years with type 1 diabetes were selected randomly. They were given NS (2gm per day) in addition to their conventional medicines- insulin - for 90 days. At day zero (prior to commencement of treatment) and at the end of the study (90 days), fasting blood glucose (FBG); glycosylated hemoglobin (HbA1c), serum urea and creatinine were checked then data was analyzed by paired *t*-test using Statistical Package for the Social Sciences (SPSS software) version 22.

**Results:** There was a significant reduction in FBG and HbA1c the P value were (0.000 and 0.003) respectively. Reduction in serum urea and creatinine was insignificant.

**Conclusion:** Our study confirmed that NS has hypoglycemic property which is reflected by reduction in both FBG and HbA1c. Non-significant alteration of urea and creatinine validate the safety of the seeds.

**Keywords:** *Nigella sativa*, Type 1 diabetic, hypoglycemia, Glycosylated hemoglobin (HbA1c).

**\*Correspondence Info:**

Dr. Malak Al-Faki Ahmed  
Department of Physiology,  
Faculty of Medicine, Nile valley university,  
Atbara, Sudan

**\*Article History:****Received:** 25/10/2019**Revised:** 24/12/2019**Accepted:** 24/12/2019**DOI:** <https://doi.org/10.7439/ijbar.v10i12.5292>**QR Code**

**How to cite:** Ahmed M, Mohammed H, Elamin NM, Musa OA. *Nigella Sativa* a Promising Drug in Treatment of Diabetes and Prevention of Its Complication. *International Journal of Biomedical and Advance Research* 2019; 10(12): e5292. Doi: 10.7439/ijbar.v10i12.5292 Available from: <https://ssjournals.com/index.php/ijbar/article/view/5292>

Copyright (c) 2019 International Journal of Biomedical and Advance Research. This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/)

**1. Introduction**

Black seeds -*Nigella sativa* (NS) - are used as a food additive and flavor in many countries [1]. NS is well known in various traditional systems of medicine like; Tibbe-Nabwi, Unani, Ayurveda and Siddha. Seeds and seeds' extracts has been used to treat many diseases all over the world [2] Many studies have showed that thymoquinone - an active ingredient of oil extracts - is responsible for most

health benefits [3,4]. Many medicinal properties and pharmacological actions of the seeds have been investigated like: bronchodilator[5], antioxidant [6], anti-inflammatory via inhibition of 5-lipoxygenase [7], anti cancer [8] and antimicrobial [9, 10], anti-diabetic activity with different mechanisms like; dose-dependent inhibition of sodium-dependent glucose transport [11], reduction of hepatic

glucose production [12], potentiation of insulin action (permissive action) [13], stimulation of insulin release (insulinotropic) [14] and amelioration in beta-cells of pancreatic islets causing an increase in insulin secretion [15] beside having antidyslipidemic effect [16] It is a beneficial plant with a wide margin of safety [17].

Diabetes mellitus is a group of metabolic disorders of carbohydrate metabolism, producing hyperglycemia. Type 1 diabetes mellitus, is caused by autoimmune destruction of the  $\beta$ -cells of the pancreas, rendering the pancreas unable to synthesize and secrete insulin. Type 2 diabetes mellitus, results from a combination of insulin resistance and inadequate insulin secretion.

There are micro and macrovascular complications caused by chronic hyperglycemia [18]. Chronic hyperglycemia leads to non-enzymatic formation of advanced glycation end products (AGEs) [19]. Some proteins in the blood like hemoglobin and albumin are susceptible to non-enzymatic attachment of free aldehyde groups of carbohydrates (such as glucose) to the unprotonated free amino groups of proteins (glycation). Glycation alters the structure of proteins [20] and interferes with their normal functions by disrupting molecular conformation, altering enzymatic activity, and interfering with receptor functioning. Recent studies suggest that AGEs interact with plasma membrane localized receptors for AGEs (RAGE) to alter intracellular signaling, gene expression, release of pro-inflammatory molecules and free radicals. AGEs plays a major role in the pathogenesis of diabetic complications including retinopathy, cataract, neuropathy, nephropathy and cardiomyopathy is also discussed [21].

Life span of RBCs is 120 days while albumin has a short half life (15-20 days). This causes HbA1c to stay in the circulation for longer time compared with albumin. This is the reason that HbA1c reflects glycemic control over a long period (2-3 months) whereas albumin does so for short time monitoring (2 weeks) [22]. HbA1c in health comprises approximately 5% of the total HbA [23]. HbA1c has been established as the gold standard index for long-term glycemic control [18].

The concept of insulin sensitivity in diabetes is attributed to Sir Harold Himsworth due to discrimination between two main types of diabetes, insulin-sensitive and insulin-insensitive diabetes [24]. In 1979 National Diabetes Data Group published diagnostic criteria and a classification system which was adopted by the World Health Organization (in 1980 with minimal changes). 140mg/dl (7.78mmol/l) was taken as a critical point to diagnose diabetes while FBG level ranging between 110mg/dl - 140mg/dl, requires Oral Glucose Tolerance Test (OGTT) for diagnosis of diabetes (diagnostic if glycaemia

>200mg/dl two hours post-OGTT). In 1997, the Expert Committee of the American Diabetes Association further revised diagnostic criteria for diabetes: the cut-off of fasting plasma glucose (FPG) was lowered from 140mg/dl (7.78mmol/l) to  $\geq 126$ mg/dl ( $\geq 7.0$ mmol/l) this change in diagnostic criteria was based on excessive population studies which showed that the incidence of rethiopathy was significantly higher even with blood glucose levels  $\geq 120$ mg/dl [18].

WHO estimates that diabetes was the seventh leading cause of death in 2016. Uncontrolled diabetes leads to serious damage to many of the body's systems [25]. Some epidemiological analyses have showed that 1% reduction in HbA1c reduces myocardial infarction, diabetes-related death and microvascular by 14%, 21% and 37% respectively. HbA1c level at or below 7% can reduce the long-term complications of the disease up to 76% [26]. The earlier detection of diabetes was minor microvascular complication [27].

## 2. Material and methods

### 2.1 Subjects:

25 patients with diabetes type 1 were selected from the outpatient clinics of Nassier Eldein diabetic center in Atbara, River Nile State, in Sudan. An ethical clearance was obtained from the hospital ethical committee before commencement of the study. Informed consents were distributed to all participants after explaining the outcomes of the treatment. A questionnaire was given to each participant. Patients were selected from the same geographical area randomly. Male / female ratio was 11:14 .

### 2.2 Materials

All patients were strictly advised to follow the guidelines regarding physical activities and diet, which were maintained as in the routine life style. Each participant was given a daily oral dose of 2g of NS. 5ml of blood collected by laboratory technician was taken for checking FBG, HbA1c, urea and creatinine at the start (day zero) and at the end of the study (after 90 days). Blood samples were taken after overnight fasting - 8 hours - with exception of water and medication. FBG was estimated by glucose oxidase method using Bio systems A25 automated clinical chemistry analyzer according to manufacturer's instructions.

## 3. Result

Male female ratio is illustrated in figure (1) and age of participants is shown in Table 1. Data was analyzed using paired t-test of (SPSS) version 22. The means of FBS, HbA1c, urea and creatinine at day zero and after three month were compared. There was a significant reduction in FBG and HbA1c (P value = 0.000, 0.003 respectively).

Illustrated in table 2. FBG and HbA1c Serum creatinine and blood urea were checked before and after and there was no significant change (P value = 0.80 and 0.64 respectively).

Figure 1: Male / Female ratio

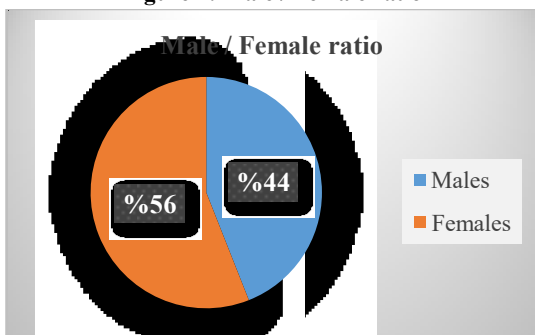


Table 1: Age of Participants

Age range	5-9	10-14	15-17
Number of Participants	8	10	7

Table 2: FBG, HbA1c, Urea and Creatinine before and after treatment

Parameter	Mean ±SD Baseline	Mean ± SD After 3month	P value
FBG(mg/dl)	287.2 ± 101.6	114. 0± 56.9	<0.001
HbA1c (%)	12.0± 2.1	8.2 ±4.2	0.003
B. urea (mg/dl)	22.12± 6.7	20.8 ± 7.6	0.64
S. creatinine (mg/dl)	0.44± 0.09	0.43 ±0.08	0.80

Figure 2: FBG Before and After Treatment

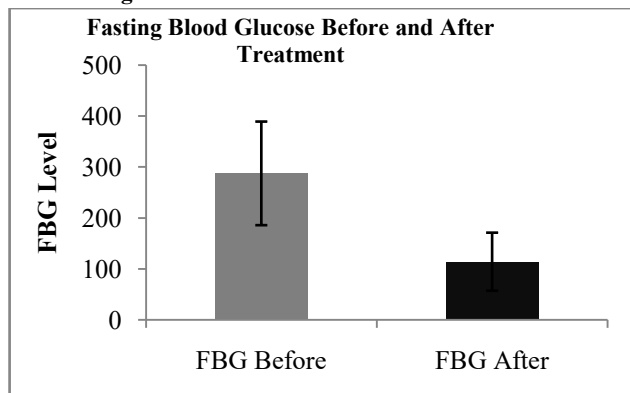
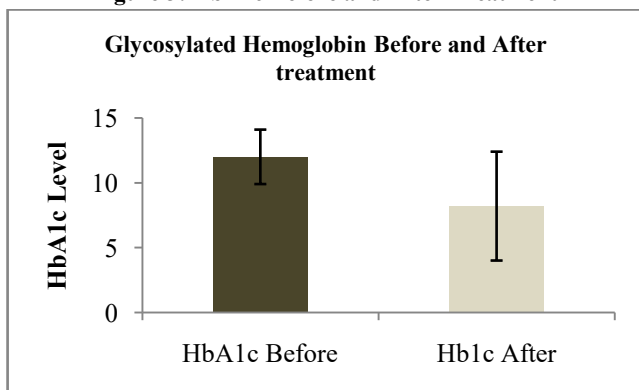


Figure 3: HbA1c Before and After Treatment



## 4. Discussion

Thymoquinone – the active ingredient of NS - is known of its antioxidant, antidiabetic and hypoglycemic properties which make this compound very effective in treatment of diabetes and prevention of its complications [6, 11-16]. The dose chosen in this study 2g/day was equivalent to one of the doses used by in Bamosa; who found that NS seeds 1, 2 and 3 g/day significantly improved glycemic control with no toxicity [28]. In this present study, we investigated hypoglycemic effect of NS in the type I diabetic patients on regular insulin treatment. Our study confirmed hypoglycemic action of NS in Type I diabetic patients when administered orally reflected by significant reduction of both FBG and HbA1c. This finding agrees with Bamosa[28], Shaafi S& Kulkarni [29] and Heshmati [30] yet, the participant in our study were type I diabetic (young 5-17 years old) compared with type II (adult) participants in the mentioned studies. ANSARI found that NS significantly improve urea and creatinine level in stage 3 and 4 chronic kidney disease CKD [31]. There was insignificant reduction of both urea and creatinine. This finding does not contradict that of ANSARI 2016 because participants in his study were suffering from CKD with too high urea and creatinine levels on the other hand it shows safety of the seeds when given in the mentioned dose and reflects that these seeds have no toxicity or side effects.

## Recommendation

More studies are to be conducted to investigate other parameters of diabetes like lipid profile and investigation of molecular mechanism by which the seeds exert their hypoglycemic effect. Also studies for longer durations are to be performed to investigate impact of NS on diabetic complications.

## References

- [1]. Hawsawi, ZA Ali BA, Bamosa AO, Effect of *Nigella Sativa* (Black Seed) and Thymoquinone on Blood Glucose in Albino Rats. *Ann Saudi Med* 2001; 21(3-4): 242-244.
- [2]. Ahmad A, Husain A, Mujeeb M, Khan SA, Najmi AK, Siddique NA, Damanhoury ZA, Anwar F. A review on therapeutic potential of *Nigella sativa*: A miracle herb. *Asian Pac J Trop Biomed.* 2013; 3(5): 337-52.
- [3]. Najmi A, Haque SF, Naseeruddin M, Khan RA. Effect of *Nigella sativa* oil on various Clinical and biochemical parameters of metabolic syndrome. *Int J Diabetes Dev Ctries.* 2008; 16:85–87.

- [4]. Kapoor S. Emerging clinical and therapeutic applications of *Nigella sativa* in gastroenterology. *World J Gastroenterol*. 2009; 7: 2170–2171.
- [5]. Salem ML, Alenzi FQ, Attia WY. Thymoquinone, the active ingredient of *Nigella sativa* seeds, enhances survival and activity of antigen-specific CD8-positive T cells *in vitro*. *Br J Biomed Sci* 2011; 68(3):131-7).
- [6]. Boskabady MH, Kiani S, Jandaghi P. Stimulatory effect of *Nigella sativa* on  $\beta$ 2-adrenoceptors of guinea pig tracheal chains *MJIRI* 2004; 18( 2): 153-158.
- [7]. Mansour MA, Nagi MN, El-Khatib AS, Al-Bekairi AM. Effects of thymoquinone on antioxidant enzyme activities, lipid peroxidation and DT-diaphorase in different tissues of mice: a possible mechanism of action. *Cell Biochem Funct* 2002; 20(2):143-51.
- [8]. Mansour M and Tornhamre S. Inhibition of 5-lipoxygenase and leukotriene C4 synthase in human blood cells by thymoquinone. *J Enzyme Inhib Med Chem* 2004; 19(5):431-6).
- [9]. Edris AE. Anti-cancer properties of *Nigella* spp. essential oils and their major constituents, thymoquinone and beta-elemene. *Curr Clin Pharmacol* 2009; 4(1): 43-6.
- [10]. Bakathir HA, Abbas NA. Detection of the antibacterial effect of *Nigella sativa* ground seeds with water. *Afr J Tradit Compl Altern Med*. 2011; 8(2): 159-164.
- [11]. Salem EM, Yar T, Bamosa AO, Al-Quorain A, Yasawy MI, Alsulaiman RM et al. Comparative study of *Nigella sativa* and triple therapy in eradication of *Helicobacter Pylori* in patients with non-ulcer dyspepsia. *Saudi J Gastroenterol*. 2010; 16(3): 207-214.
- [12]. Meddah B, Ducroc R, El Abbes Faouzi M, Eto B, Mahraoui L, Benhaddou-Andaloussi A, Martineau LC, Cherrah Y, Haddad PS. *Nigella sativa* inhibits intestinal glucose absorption and improves glucose tolerance in rats. *J Ethnopharmacol* 2009; 121(3): 419-24.
- [13]. 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(3):219-23.
- [14]. Najmi A, Nasiruddin M, Khan RA, Haque SF. Effect of *Nigella sativa* oil on various clinical and biochemical parameters of insulin resistance syndrome. *Int J Diab Dev Ctries* 2005; 28 (1): 11-4.
- [15]. Rhid H, Chevassus H, Nmila R, Guiral C, Petit P, Chokairi M, Sauvaire Y. *Nigella sativa* seed extracts enhance glucose-induced insulin release from rat-isolated Langerhans islets. *Fundam Clin Pharmacol* 2004; 18(5): 525-9.
- [16]. 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(4):213-9.
- [17]. Kocyigit Y, Atamer Y, Uysal E. The effect of dietary supplementation of *Nigella sativa* L. on serum lipid profile in rats. *Saudi Med J* 2009; 30(7): 893-6
- [18]. Al-Ali A, Alkhawajah AA, Randhawa MA, Shaikh NA. Oral and intraperitoneal LD50 of thymoquinone, an active principle of *Nigella sativa*, in mice and rats. *J Ayub Med Coll Abbottabad* 2008; 20(2):25-7.
- [19]. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2011; 34 (1):S62-9.
- [20]. Fowler. M. J. Microvascular and Macrovascular Complications of Diabetes. *Clinical Diabetes* 2011; 29(3):116-122.
- [21]. Makris K, Spanou L. Is there a relationship between mean blood glucose and glycated hemoglobin? *J Diabetes Sci Technol*; 2011; 5(6):1572-83.
- [22]. Singh VP, Bali A, Singh N, Jaggi AS. Advanced glycationend products and diabetic complications. *Korean J Physiol Pharmacol* 2014; 18(1):1-14.
- [23]. Takahashi S, Uchino. H, Himizu. T, Kanazawa. A, Tamura Y, Sakai. K, Watada. H, Hirose. T, Ryuzo Kawamori. R, Tanaka. Y. Comparison of glycated albumin (GA) and glycated hemoglobin (HbA1c) in type 2 diabetic patients: usefulness of GA for evaluation of short-term changes in glycemic control. *Endocrine Journal* 2007; 54(1): 139-144.
- [24]. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. *Biomark Insights* 2016; 11:95-104.
- [25]. Gale E. A. M. Commentary: The hedgehog and the fox: Sir Harold Himsworth (1905–93). *International Journal of Epidemiology*, 2013; 42 (6): 1602–1607.
- [26]. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2003; 26 Suppl 1: S5-20.
- [27]. Najafipour F, Mobasser M Yavari A, Nadrian H, Aliasgarzadeh A, Mashinchi Abbasi N, Niafar M, Houshyar Gharamaleki J, Sadra V. Effect of regular exercise training on changes in HbA1c, BMI and VO2max among patients with type 2 diabetes mellitus: an 8-year trial *BMJ Open Diabetes Res Care*. 2017; 5(1): e000414
- [28]. DECODE Study Group on Behalf of the European Diabetes Epidemiology Study Group: Will new diagnostic criteria for diabetes mellitus change

- phenotype of patients with diabetes? Reanalysis of European epidemiological data. *BMJ* 1998; 317: 371–375.
- [29]. 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(4): 344–354.
- [30]. Shaafi S M, Kulkarni H. Effect of Kalonji (N. Sativa) Seeds on Glycemic Control of Patients with Type-2 Diabetes. *SSRG International Journal of Medical Science* 2017; 4(3).
- [31]. Heshmati J, Namazi N, Memarzadeh M, Taghizadeh M and Kolehdooz F. “*Nigella sativa* oil affects glucose metabolism and lipid concentrations in patients with type 2 diabetes: A randomized, double-blind, placebo-controlled trial”. *Food Research International* 2015; 70 : 87-93.
- [32]. Ansari. Z M, Nasiruddin. M, Khan. R. A, Haque. S.F. Evaluation of Efficacy and Safety of *Nigella Sativa* Oil Supplementation in Patients of Chronic Kidney Disease. *Asian J Pharm Clin Res*, 2201; 9 (2): 107-110.