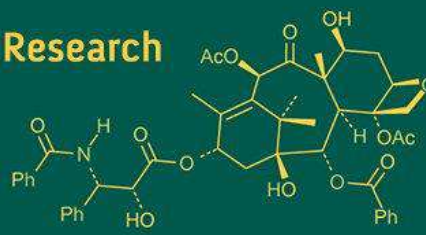
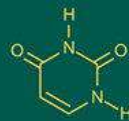
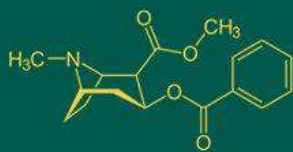


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## Effect of daily consumption of *Nigella sativa* seed on serum lipids in adult subjects

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### Abstract

**Background:** The lipid lowering effects of *Nigella sativa* extracts have been reported in numerous research works. In Benin, *Nigella sativa* seeds are consumed by the population in order to treat various ailments and diseases.

**Objective:** This study aimed to assess the effect of daily consumption of *Nigella sativa* seed on serum lipids in adult subjects.

**Methods:** This research work, being an interventional study of quasi-experimental category, involved 67 voluntary adult subjects (mean age: 33.51±11.40 years; 32 men; 35 women), conducted in Parakou (Benin), from January 15 to April 14, 2021. Each subject consumed per day two (2) grams of *Nigella sativa* seed powder for 90 consecutive days. The lipid parameters were measured before starting the experiment, and then during all the 30 days. Student's t-test helped compare the averages of lipid parameters at the threshold of 5%.

**Results:** The intake of *Nigella sativa* seed powder reduced significantly total cholesterol (1.83±0.47 g/L vs. 1.64±0.32 g/L; P=0.000), LDL cholesterol (1.08±0.44 g/L vs. 0.90±0.29 g/L; P=0.000) and triglycerides (1.01±0.60 g/L vs. 0.87±0.48 g/L; P=0.003). HDL cholesterol experienced a non-significant increase (0.53±0.19 g/L vs. 0.56±0.12 g/L; P=0.146) within a range of 5.70%. The following rates of decline were noted: total cholesterol (10.40%), LDL cholesterol (16.70%) and triglycerides (13.90%).

**Conclusion:** At the end of the 90 days, the *Nigella sativa* seed powder improves the lipid profile in the adult subject. Its consumption may be helpful in the prevention and management of dyslipidemias.

**Keywords:** Lipids, cholesterol, triglycerides, *Nigella sativa*

### Introduction

Dyslipidemias are one of the main biological risk factors for cardiovascular diseases (CVDs) [1]. In Africa, CVDs have become a public health concern which requires early diagnosis, adequate management and overall prevention [2]. In Benin, dyslipidemias' prevalence was 82% among patients with sickle cell disease [3] and 86.98% among menopausal women [4].

The management of dyslipidemias requires dietary measures and drug therapy which may be burdensome for the patients, because of their high cost [5]. Likewise, the complications related to patients' non-compliance with therapy and high tendency to consume medicinal plants have led the World Health Organization to encourage the use of plants with potential healing properties in order to facilitate the improvement of patients' health and autonomy [6]. The medicinal plants provide a substantial variety of treatments and some of them have an impact on serum lipid profile.

*Nigella sativa* (family: Ranunculaceae; genus: *Nigella*) is a medicinal plant used for the treatment of various diseases in different regions of the world. It grows on semiarid lands and is widely cultivated in Europe, Syria, Egypt, Saudi Arabia, Turkey, Iran, Pakistan and in India [7]. *Nigella sativa* is effective against cancer, diabetes, asthma, it is gastro-protective and has effects on fertility; it is diuretic, antispasmodic, anti-inflammatory and analgesic, antimicrobial, antifungal, anthelmintic, anticonvulsant, anxiolytic, neuroprotective, nephroprotective, an hepatoprotective agent, cardioprotective and immunomodulator [8-10]. The lipid lowering effects of *Nigella sativa* extracts in normal and diabetic animals as well as in humans have been reported in various research works [11-14].

In Benin, *Nigella sativa* seeds are sold in markets and consumed by the populations in order to treat many illnesses and ailments.

This study aimed to appraise the effect of daily consumption of *Nigella sativa* seed on serum lipids among adult subjects in order to seek an alternative solution for drug therapy within the framework of the treatment of different types of dyslipidemia.

## Materials and Methods

### Type and period of study

This research work is an interventional study of quasi-experimental category. The data used in this study were collected from January 15 to April 14, 2021.

### Study subjects

The sample consisted of adult subjects aged 18 to 60 years, from both sexes, volunteers, selected after their informed, read, and approved consent. They lived in Parakou (Republic of Benin) during the period of data collection and presented with normal baseline kidney and liver function test. Chronic alcohol-dependent subjects, suffering from a liver disease or a kidney disease, as well as pregnant and breastfeeding women were excluded. The study also excluded subjects with incomplete follow-up (those who did not keep monthly appointments), those who withdrew from the study or presenting with an ongoing or evolutive pregnancy after the start of the study. 67 adult subjects (32 men and 35 women) meeting the inclusion criteria, were recruited through a complete census.

### Plant material

The plant material consisted of *Nigella sativa* seeds bought in the markets of Benin and Niger. These seeds were identified at the Botany Laboratory of the Faculty of Agricultural Sciences of the University of Parakou (Prof. Honoré BIAOU, CAMES Professor) and ground to powder and stored in brown glass bottles tightly sealed.

### Data collection

The data were collected by means of a written questionnaire and direct interview, including the following items: sociodemographic data, anthropometric measurements (weight, size, waist circumference, hip circumference and blood pressure), and biochemical parameters (total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides).

### Experiment

At the beginning of the experiment, each selected subject benefitted from the measurement of anthropometric parameters and lipid parameters (total cholesterol, HDL cholesterol, triglycerides and LDL cholesterol). Then, each subject consumed every day two (2) grams of *Nigella sativa*

seed powder for 90 consecutive days, without taking into account the time of the day and feeding. Eventually, the same lipid parameters as the initial ones were measured every 30 days during the 90 days. During the experiment, each subject involved in the study maintained his/her usual lifestyle.

### Measurement of lipid parameters

The blood samples (4 mL in dry tube) to be used for measuring the lipid parameters were collected in the morning among the subjects fasting for at least 12 hours. The blood samples thus collected underwent centrifugation at 4000 revolutions per minute for 5 minutes, and then serums were decanted. The total cholesterol has been measured using cholesterol oxidase endpoint enzyme assay [15], HDL cholesterol by means of phosphotungstic acid precipitation procedure in the presence of magnesium ions [16], and triglycerides through endpoint enzyme assay using glycerol phosphate oxidase [17]. LDL cholesterol has been determined by computation using the formula of Friedewald *et al.* [18] under the conditions of triglyceride levels lower than 3.5 g/L. The atherogenic index of plasma (AIP) has been computed using the formula  $\log(\text{triglycerides}/\text{HDL cholesterol})$  [19].

### Data analysis

The software SPSS 26 (IBM corps, 2019) was used to perform data analysis and processing. The quantitative variables were expressed as averages  $\pm$  standard deviation when distribution is normal, and the qualitative ones as population size (number of subjects) and percentages. Student's t-test was used to compare averages. The analysis of variance (ANOVA) permitted to compare the mean values of lipid parameters of the four periods. This comparison has been made between the values obtained before the consumption of *Nigella sativa* seed powder and those obtained every 30 days during the 90 days. The Significance level was set at 0.05.

### Ethical considerations

The research protocol of this study was approved by the Ethics Local Committee for Biomedical Research of the University of Parakou (Opinion No. 0388/CLERB-UP/P/SP/R/SA).

### Results

#### General characteristics of the study subjects

Table 1 shows the general characteristics of the 67 subjects selected. Men were taller than women ( $P=0.000$ ) whereas women were older ( $P=0.036$ ) and had a higher body mass index ( $P=0.001$ ), waist circumference ( $P=0.028$ ) and hip circumference ( $P=0.001$ ).

**Table 1:** General characteristics of the study subjects

	Total (N=67)	Men (n=32)	Women (n=35)	P
Age (years)	33.51 $\pm$ 11.40	30.47 $\pm$ 10.71	36.29 $\pm$ 11.44	0.036
Weight (kg)	68.88 $\pm$ 16.75	67.16 $\pm$ 15.12	70.45 $\pm$ 18.19	0.425
Height (cm)	1.66 $\pm$ 0.09	1.73 $\pm$ 0.07	1.61 $\pm$ 0.05	0.000
BMI (kg/m <sup>2</sup> )	24.99 $\pm$ 6.31	22.48 $\pm$ 4.56	27.29 $\pm$ 6.85	0.001
Waist circumference (cm)	87.28 $\pm$ 17.00	82.55 $\pm$ 15.08	91.60 $\pm$ 17.71	0.028
Hip circumference (cm)	99.13 $\pm$ 14.27	93.30 $\pm$ 11.06	104.46 $\pm$ 14.92	0.001
Systolic BP (mmHg)	124.18 $\pm$ 26.06	119.06 $\pm$ 12.54	128.86 $\pm$ 33.59	0.115
Diastolic BP (mmHg)	81.04 $\pm$ 16.71	80.31 $\pm$ 10.62	81.71 $\pm$ 20.93	0.728

BMI = body mass index; BP = blood pressure; P = Student's t-test; the table values are expressed as averages  $\pm$  standard deviation

### Serum lipid parameters

Among men, at the end of 90 days, *Nigella sativa* seed powder reduces significantly total cholesterol ( $P=0.000$ ), LDL cholesterol ( $P=0.000$ ) and serum triglycerides ( $P=0.020$ ). As regards HDL cholesterol, a non-significant

increase was noted ( $P=0.648$ ) (Table 2). Total cholesterol, triglycerides and LDL cholesterol, respectively decreased by 11.70%, 14.67% and 18.20% at the end of the 90 days of consumption of *Nigella sativa* seed powder, unlike HDL cholesterol by an average that slightly increased by 2.50%.

**Table 2:** Lipid parameters (average  $\pm$  standard deviation) of the 32 male subjects during the 90 days of consumption of *Nigella sativa* seed powder

	D0	D30	D60	D90	P*(M0-M3)	P (M0-M3)
Total cholesterol (g/L)	1.74 $\pm$ 0.49	1.67 $\pm$ 0.37	1.59 $\pm$ 0.32	1.53 $\pm$ 0.30	0.000	0.000
HDL cholesterol (g/L)	0.51 $\pm$ 0.16	0.55 $\pm$ 0.15	0.50 $\pm$ 0.12	0.53 $\pm$ 0.10	0.176	0.648
Triglycerides (g/L)	0.96 $\pm$ 0.50	0.85 $\pm$ 0.42	0.84 $\pm$ 0.41	0.82 $\pm$ 0.51	0.091	0.020
LDL cholesterol (g/L)	1.03 $\pm$ 0.50	0.94 $\pm$ 0.40	0.92 $\pm$ 0.32	0.84 $\pm$ 0.32	0.002	0.000

P\*(M0-M3) = ANOVA; p (M0-M3) = Student's t-test; D = day

In women, at the end of the 90 days of consumption of *Nigella sativa* seed powder, a significant decrease of total cholesterol ( $P=0.001$ ), LDL cholesterol ( $P=0.001$ ) and triglycerides ( $p=0.048$ ) had been noted. HDL cholesterol increased in a non-significant manner ( $P=0.123$ ) (Table 3).

Total cholesterol, triglycerides and LDL cholesterol declined respectively by 9.20%, 13.70% and 15.10% after 90 days, in contrast with HDL cholesterol the average of which increased by 7.70% during the same period.

**Table 3:** Lipid parameters (average  $\pm$  standard deviation) of the 35 female subjects during the 90 days of consumption of *Nigella sativa* seed powder

	D0	D30	D60	D90	P*(M0-M3)	P(M0-M3)
Total cholesterol (g/L)	1.91 $\pm$ 0.44	1.86 $\pm$ 0.43	1.79 $\pm$ 0.32	1.74 $\pm$ 0.31	0.002	0.001
HDL cholesterol (g/L)	0.56 $\pm$ 0.22	0.63 $\pm$ 0.17	0.57 $\pm$ 0.121	0.60 $\pm$ 0.13	0.028	0.123
Triglycerides (g/L)	1.05 $\pm$ 0.69	0.98 $\pm$ 0.54	0.88 $\pm$ 0.45	0.91 $\pm$ 0.47	0.050	0.048
LDL cholesterol (g/L)	1.13 $\pm$ 0.39	1.01 $\pm$ 0.36	1.05 $\pm$ 0.25	0.96 $\pm$ 0.26	0.004	0.001

P\* (M0-M3) = ANOVA; P (M0-M3) = Student's t-test; D = Day

At the end of the experiment, the intake of *Nigella sativa* seed powder reduced significantly total cholesterol ( $P=0.000$ ), LDL cholesterol ( $P=0.000$ ) and triglycerides ( $P=0.003$ ) among all the 67 subjects involved in the study. HDL cholesterol experienced a non-significant increase

( $P=0.146$ ) (Table 4). The mean values of total cholesterol, triglycerides and LDL cholesterol declined respectively by 10.40%, 13.90% and 16.70%, unlike HDL cholesterol with an average that slightly increased by 5.70% in the same period.

**Table 4:** Lipid parameters (average  $\pm$  standard deviation) of the 67 subjects during the 90 days of consumption of *Nigella sativa* seed powder

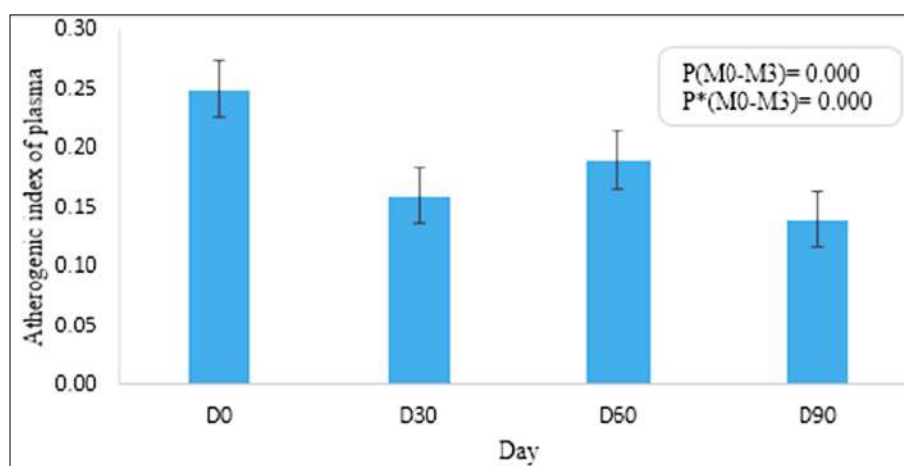
	D0	D30	D60	D90	P*(M0-M3)	P(M0-M3)
Total cholesterol (g/L)	1.83 $\pm$ 0.47	1.76 $\pm$ 0.41	1.69 $\pm$ 0.33	1.64 $\pm$ 0.32	0.000	0.000
HDL cholesterol (g/L)	0.53 $\pm$ 0.19	0.60 $\pm$ 0.17	0.53 $\pm$ 0.12	0.56 $\pm$ 0.12	0.065	0.146
Triglycerides (g/L)	1.01 $\pm$ 0.60	0.92 $\pm$ 0.48	0.86 $\pm$ 0.43	0.87 $\pm$ 0.48	0.322	0.003
LDL cholesterol (g/L)	1.08 $\pm$ 0.44	0.98 $\pm$ 0.38	0.99 $\pm$ 0.29	0.90 $\pm$ 0.29	0.449	0.000

P\* (M0-M3) = ANOVA; P (M0-M3) = Student's t-test; D = day

### Atherogenic index of plasma

At the end of the experiment, the atherogenic index of

plasma declined significantly among the 67 subjects ( $P=0.000$ ), within a range of 44% (Figure 1).



**Fig 1:** Atherogenic index of plasma of the 67 subjects during the 90 days of consumption of *Nigella sativa* seed powder

P\* (M0-M3) = ANOVA; P (M0-M3) = Student's t-test; D = day

## Discussion

As demonstrated in this study, many experimental works carried out in humans have pointed out a lowering of total cholesterol, LDL cholesterol and triglycerides do with consumption of *Nigella sativa* seed. A meta-analysis of 50 randomized clinical trials has reported a significant reduction of total cholesterol, triglycerides, LDL cholesterol and VLDL cholesterol after a *Nigella sativa* supplementation [20]. In another meta-analysis of 7 trials, the consumption of *Nigella sativa* seed oil resulted in a significant reduction of triglycerides [13]. A randomized, double clinical trial has noted a significant decrease of triglycerides and LDL cholesterol in the therapy control group compared to the placebo group after 12 weeks for processing of *Nigella sativa* seed [12]. Among the patients with type 2 diabetes who ingested per day during 12 weeks 2 g of *Nigella sativa* seed, a significant lowering of total cholesterol, LDL cholesterol, triglycerides and an increase of HDL-C/LDL-C ratio with respect to control cases, have been found out [21]. As in this study, some authors have found out that the *Nigella sativa* seed powder caused a non-significant increase of HDL cholesterol [11, 14]. Among a population of diabetic subjects, a significant elevation of HDL cholesterol has been observed after 4 weeks of intake of 1 g per day of *Nigella sativa* seed [21]. Among the diabetic rats treated during 8 weeks with 2 g/kg of aqueous extract of *Nigella sativa* seed, a significant increase of HDL cholesterol has been noted [22]. In this research work, the rate of decrease of lipid parameters varied between 10.40% and 16.70%; an increase estimated at 5.70% has been noted for HDL cholesterol. The same trend has been reported by other authors [12, 21].

The lipid lowering effect of *Nigella sativa* seed is clearly demonstrated. It does not seem to be due to only one phytochemical, but rather to the synergistic action of several phytochemical compounds that it contains i.e. thymoquinone, sterols, flavonoids and polyunsaturated fatty acids [23]; the said effect is also due to nigellamine which has the potential to lower triglycerides' levels [24]. Thymoquinone has a lipid lowering effect in diabetic rats, according to two mechanisms, i.e. by increasing the capture of LDL cholesterol via a regulation of hepatic low-density lipoprotein (LDL) receptor gene, and by reducing the activity of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase which is the enzyme that controls cholesterol biosynthesis [25]. The triglyceride lowering effect of phyosterols is due not only to the reduction of VLDL production by the liver [26] but also to the reduction of de novo lipogenesis [27]. Through the inhibition of the activities of HMG-CoA reductase and hepatic Acyl-Coenzyme A Cholesterol Acyltransferase (ACAT), flavonoids reduce plasma cholesterol concentrations [28]. Nigellamine A5 would bring about increased catabolism of triglyceride-rich particles, and reduction of VLDL secretion, resulting in the reduction of plasma triglycerides [29].

In this study, the consumption of *Nigella sativa* seed powder reduces the atherogenic index of plasma (AIP) significantly. The administration of thymoquinone to diabetic rats during three weeks resulted in a significant decrease of the AIP [30]. The AIP is a marker that enables to predict risk for atherosclerosis and cardiovascular diseases. The significant decrease of AIP through intake of *Nigella sativa* seed associated with the lipid lowering effects identified in this study confirm the status of a cardioprotective agent of the said seed reported in the literature [8-10].

## Conclusion

The results of this study revealed that the daily consumption of *Nigella sativa* seed powder reduces the plasma concentrations of total cholesterol, LDL cholesterol and triglycerides but increases HDL cholesterol after ninety days. In addition, a reduction of the AIP is noted. The *Nigella sativa* seed may be helpful in preventing and treating different types of dyslipidemia, and thereby in reducing the risk for cardiovascular diseases.

## Conflict of interest

The authors have not declared any conflict of interest.

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