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Preliminary Study to Evaluate the Health Benefits of Natural(Crude) *versus* Commercial black seed oil in Sample of Healthy volunteers

Doa'a Anwar Ibrahim*

Department of Pharmacology, University of Science and Technology, Sana'a, Yemen

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Abstract

Plants had been used for medicinal purposes long before recorded history. The seeds of Nigella sativa Linn. (Ranunculaceae), commonly known as black seed or black cumin, are used in folk (herbal) medicine all over the world for the treatment and prevention of a number of diseases.Black seed is recommended by the Prophet Muhammad (SWS): The beard hair of the Holy Prophet (peace be upon him). "Hold on to the use of the black seed for indeed it has a remedy for every disease except death." This study is aimed to compare between natural (crude) versus commercial black seed oil through measuring some parameters: liver function enzymes (SGOT and SGPT), CBC as well as FBS.Methodology: 20 healthy volunteers were divided randomly to 3 groups (I, II and III). Group I (n=8) was allowed to take natural (crude) black seed oil (2 teaspoonful/d), Group II (n=8) was allowed to take commercial ANSO-SYP black seed oil (Nigoil) (2 teaspoonful/d), group III (n=6) was kept as placebo only taken (2 teaspoonful/d of sun flower oil) for two weeks. Washout period was done for all groups for two weeks. Cross over between group I and II was done in this part, where group I (n=8) was allowed to take natural (crude) black seed oil (2 teaspoonful/d), group II (n=8) was allowed to take commercial ANSO3 Phenomenal®soft gelatin capsule (2 capsules/d), group III (n=6) was kept as placebo only taken (2 teaspoonful/d of sun flower oil) for two weeks.Blood sample was taken before (baseline) starting this study and at the end of study. The following parameters were measured complete blood count CBC hepatic function enzymes (SGOT and SGPT) and fasting blood sugar. Results: commercial black seed oil especially(soft gelatin capsule) showed significant increase ($p<0.05$) fasting blood sugar as compared with natural (crude) black seed oil and placebo, while natural oil showed reduction in FBS.Conclusion: commercial black seed oil especially soft gelatin capsule showed significant increase in fasting blood sugar. This may referred to the presence of impurities.

Key words: Natural(crude) black seed; Commercial black seed; Liver function enzymes; Complete blood count; Fasting blood sugar.

***Corresponding author**
Doa'a Anwar Ibrahim
Department of Pharmacology,
University of Science and Technology
Sana'a, Yemen
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Contents

1. Introduction

The last two decades witnessed an enormous research rush to reveal the pharmacological actions of an annual spicy delicate and beautiful herb known by the Latin name Nigella sativa Linnaeus variety hispidula (brachyloba [1] .Nigella sativa is a herbal plant which belongs to Ranunculaceae family. It is a native of southern Europe. It is found all over India and is specially seen in the eastern region and also in Arab countries [2].

The seeds contain a brown colored volatile oil 0.5 % to 1.6 % mainly thymoquinone and nigellone and red colored stable oil which is 31 %. Besides this it contains albumin, sugar, carbonic acid, seponin, melanthin, Arabic acid, a bitter compound named nigellin, resins, tennins and ash 7 %. It contains a volatile oil carvone 45 to 60 %, D-lymonine and cymine[3]. They are acrid, bitter, thermogenic, aromatic, carminative, diuretic, antibacterial, deodorant, appetizing, digestive, anthelmintic, constipating, febrifuge, stimulant, galactagogue, and expectorant. They are useful in skin diseases, hemorrhoids, jaundice, inflammation (through Inhibition of thromboxane A2 and LTB4 and leukocytes), fever, paralysis, ophthalmia, halitosis, anorexia, dyspepsia, flatulence, diarrhea, dysentery, cough, amenorrhea, dysmenorrhea and helminthiasis, especially tapeworm. Moreover, seeds have benefits on heart [4], respiratory system[5,6, 7],improve and protect gastric ulcer [8,9], insulin secretagouge [10, 11, 12]and hepatoprotective effect [13, 14]. Moreover, black seed oil particularly thymoquinone (TQ) has protective effect against cisplatin- induced nephrotoxicity [15].

In 2005, Rooney and Ryan [16] found that although TQ exerted cytotoxicity against lungs, larynx, colon and pancreas carcinomas yet it was more potent against the larynx ones. In a later investigation, the authors delineated the TQ-induced cytotoxicity being due to the depletion of cellular glutathione and the activation of caspase-3 enzyme [17]. The aim of this study is to evaluate the health benefits of natural (crude) compared with that of commercial black seed oil through measuring some parameters in healthy volunteers including : Complete blood count (CBC), hepatic function enzymes including (SGOT and SGPT) and fasting blood sugar (FBS).

2. Materials and Methods

2.1.Materials

2.1.1.Participants: 20 Healthy volunteers with age range from (22-24 years old) were participated in this study. They were kept under standard situation and excluded intake herbs, drinks or medications that may interfere with the outcomes of this study.

2.1.2.Drugs: Natural Nigella sativa(Black seeds) was purchased from special Herb stores , Sana'a City and taken to squeezing stores to get the pure crude oil after identification by botanist in Pharmacognosy department –UST, ANSO3 Phenomenal®soft gelatin capsule was purchased from BLUE BIOTECH INT. Germany and ANSO-SYP black seed oil (Nigoil) was purchased from Refal Co. with A.U.F-GMBH- Germany.

2.2. Study design

20 healthy volunteers were divided randomly to 3 groups (I, II and III). Group I (n=8) was allowed to take natural (crude)black seed oil (2 teaspoonful/d), Group II (n=8) was allowed to take commercial ANSO-SYP black seed oil (Nigoil) (2 teaspoonful/d), group III (n=6) was kept as placebo only taken (2 teaspoonful/d of sun flower oil). Washout period was done for all groups for two weeks. Cross over between group I and II was done in this part, where group I (n=8) was allowed to take natural (crude) black seed oil (2 teaspoonful/d), group II (n=8) was allowed to take commercial ANSO3 Phenomenal®soft gelatin capsule (2 capsules/d), group III (n=6) was kept as placebo only taken (2 teaspoonful/d of sun flower oil) for two weeks. Blood samples were taken before (baseline) starting this study and after two weeks of experiment and washout period. The following parameters were measured complete blood count CBC (AXSYM XT-2000-ROCH), hepatic function enzymes (SGOT [18] and SGPT [19]) and fasting blood sugar[20]. All this cross over study's procedure was in accordance with the guidelines for the human, and approval from the Institutional Research and Ethics Committee, UST was received prior to the experiments.

Statistical analysis

Results were expressed as mean ± s.e.m. (standard error of mean). Statistical difference was calculated by the students' t-test and $p<0.05$ was considered as statistically significant.

3. Results and Discussion

Table 1. Effect of natural black seed oil and commercial oil and soft gelatin capsule on average (M±SE) hepatic function

Parameters / Groups	Natural (crude oil)		Commercial ANSO-SYP black seed oil (Nigoil)		Placebo	
	Before	After	Before	After	Before	After
SGOT (U/L)	18.83±1.60	18.0±1.61	18.5±1.05	17.7±1.38	17.5±0.64	17.6±1.20
SGPT (U/L)	15.16±2.27	14.66±2.3	14.33±1.49	13.5±2.07	14.1±1.66	15.0±2.30
Washout period for 2 weeks						
Parameters / Groups	Natural (crude oil)		ANSO3 Phenomenal® soft gelatin capsule		Placebo	
	Before	After	Before	After	Before	After
SGOT (U/L)	17.8±0.98	18.0±1.23	15.1±2.27	16.66±2.70	15.9±3.2	16.44±0.78
SGPT (U/L)	14.8±1.77	13.5±2.07	14.66±1.20	14.66±1.20	13.00±1.21	14.27±1.08

Insignificant change with P-value > 0. 05

Table 2. Effect of natural black seed oil and commercial oil and soft gelatin capsule on average (M±SE) fasting blood sugar in healthy volunteers (n=20)

Parameters / Groups	Natural (crude oil)		Commercial ANSO-SYP black seed oil (Nigoil)		Placebo	
	Before	After	Before	After	Before	After
FBS(mg/dl)	90.0±1.46	80.3.±4.84*	94.6±1.52	91.5±2.8	87.2±1.25	89.5±1.61
p-value		0.015		0.26		0.40
Washout period for 2 weeks						
Parameters / Groups	Natural (crude oil)		ANSO3 Phenomenal® soft gelatin capsule		Placebo	
	Before	After	Before	After	Before	After
FBS(mg/dl)	91.2±1.44	79.1±0.90*	93.0±2.08	102.0±1.57*†	89.8±1.39	89.0±2.68
p-value		0.01		0.04		0.33

*Significant as compared with control (Before) at P<0.05, †Significant as compared with Natural NS oil at P<0.05

Table 3. Effect of natural black seed oil and commercial oil and soft gelatin capsule on average (M±SE) complete blood count (CBC) in healthy volunteers (n=20)

Parameters / Groups	Natural (crude oil)		Commercial ANSO-SYP black seed oil (Nigoil)		Placebo	
	Before	After	Before	After	Before	After
Hb(g/dl)	14.58±0.41	14.87±0.54	15.33±0.45	15.25±0.47	13.5±0.311	13.8±0.25
PCV%	43.5±1.23	44.3±1.49	46.0±1.21	45.8±1.44	41.5±0.64	42.6±0.61
RBC X10×12/L	5.27±0.061	5.26±0.098	5.28±0.08	5.55±0.05	5.12±0.1	5.31±0.17
MCV (Femto liters)	83.33±1.40	83.83±1.27	85.66±1.90	85.00±1.31	81.0±0.91	80.1±2.8
MCH (pg)	27.3±0.80	27.5±0.80	29.3±0.98	27.5±0.80	26.7±0.47	26.1±1.24
MCHC (g/dl)	32.67±0.42	32.5±0.43	34.3±0.55	32.3±0.49	32.7±0.48	32.4±0.50
T.WBCX10×9/L	7.12±1.12	6.40±1.37	7.4±0.95	6.53±1.23	5.46±0.62	5.66±0.67
PlateletsX10^9/L	263.3±20.3	268.0±19.29	250.8±13.5	261.0±16.4	307.8±29.7	305.8±44.0
Washout period for 2 weeks						
Parameters / Groups	Natural (crude oil)		ANSO3 Phenomenal® soft gelatin capsule		Placebo	
	Before	After	Before	After	Before	After
Hb(g/dl)	15.0±0.36	15.3±0.36	14.38±0.48	14.83±0.45	14.68±0.322	14.75±0.41
PCV%	43.4±0.649	43.28±0.83	43.5±0.84	44.5±1.31	46.0±1.21	45.8±1.44
RBC X10×12/L	5.28±0.09	5.25±0.12	5.13±0.033	5.37±0.076	5.28±0.08	5.55±0.05
MCV(Femtoliters)	85.66±1.90	85.00±1.31	84.83±1.40	84.16±1.51	85.66±1.90	85.00±1.31
MCH (pg)	27.6±0.76	27.5±0.84	28.1±0.87	27.6±0.76	27.85±0.67	28.0±0.72
MCHC (g/dl)	32.8±0.47	32.6±0.42	33.1±0.40	32.6±0.33	33.85±0.40	34.0±0.37
T.WBCX10×9/L	6.13±0.97	6.21±0.73	6.33±1.10	5.81±0.96	5.64±0.63	5.90±0.54
PlateletsX10^9/L	264.1±26.8	317.8±37.3	6.33±1.10	5.81±0.96	5.64±0.63	5.90±0.54

Discussion

The oil of crude nigella sativa is so beneficial due to its content of over a hundred components such as aromatic oils, trace elements, vitamins and enzymes. It contains 58% of essential fatty acids including omega 6 and omega 3. These are necessary for the forming of Prostaglandin E1 which balances and strengthens the immune system giving it the power to prevent infections and allergies and control chronic illnesses. Healthy cells are protected from viruses thus inhibiting tumors. Blackseed oil also contains about 0.5 – 1.5% volatile oils including nigellone and thymoqinone which are responsible for its anti-histamine, anti-oxidant, anti-infective and gastroprotetive effect[4,8]. Outcomes of this study showed that neither natural (crude) nor commercial black seed oil have any change on liver function enzymes as well as complete blood count.

Ali BH, Blunden G, 2003 disagreed with our findings. He found that treatment of rats with the seed extract for up to 12 weeks induce changes in the haemogram that include an increase in both the packed cell volume (PCV) and haemoglobin (Hb), and a decrease in plasma concentrations of cholesterol, triglycerides and glucose [21]. Moreover, preliminary evidence suggests that oil may help minimize chemotherapy-induced decreases in hemoglobin and leukocyte counts. It helps with the process of thrombosis inside and external side of the body, ensuring that clotting of blood happens quickly to prevent further loss of blood from the injured parts of the body. It also controls fibrin to prevent excessive coagulation of blood and to ensure smooth flow of blood in the arteries and veins [22]. In addition, Enomoto et al., 2001showed that some aromatic compounds present in the extract were found to be more potent than aspirin, which is well known as a remedy for thrombosis [23].

In many Arab countries N. sativa and its derived products are consumed abusively for traditional treatment of blood homeostasis abnormalities and as a treatment for dyslipidemia [24].Our results were supported by other studies. They referred the hepatoprotective of NS to the presence of thymoquinone (TQ)as an active constituent in NS. In fact, the antioxidant and free radical scavenging properties of many144 Lead molecules from natural products: discovery and new trends plants have been found to play an important role in their hepatoprotective activity [25, 26, 27, 28].Oxidant stress can increase the susceptibility to irreversible injury by oxidative intoxication and by free radicals that can result in lipid peroxidation, protein oxidation,protein inactivation, disturbance in calcium homeostasis and consequent loss of cell viability [29, 30].

In this study, crude oil showed significant reduction in fasting blood sugar. Controversially, commercial NS capsule showed unexpected significant elevation in the level of fasting blood sugar compared with baseline measurement (before), natural (crude) as well as placebo group. There is no clear or exact explanation of this effect. It may refer to the presence of traces amount of impurities. Traditionally N. sativa plant has been used in many Middle Eastern countries as a natural remedy for diabetes. Significant reduction in blood glucose and cholesterol levels in humans following the use of the plant was reported [31, 32, 33] to elucidate the mechanism of this antidiabetic action, the rate of gluconeogenesis in isolated hepatocytes as well as the activity of pyruvate carboxylase and phosphoenolpyruvate carboxykinase in rat liver homogenates was examined. Extracts of this plant showed significant decreased in hepatic gluconeogenesis. Similar insulinotropic effects of NSO were recently observed instreptozotocin plus nicotinamide-induced diabetes mellitus in hamsters (a model of type 2 diabetes) orally fed with the oil (Fararh et al., 2002) [34].

In this study, positive immunoreactivity for the presence of insulin was observed in the pancreases from oil-treated vs. non-treated hamsters using immunohistochemical staining, suggestingthat the hypoglycemic effect of NSO resulted, partly, from a stimulatory effect onbeta cell function with consequent increase in serum insulin level. The ability of NSO to lower blood glucose concentrations was later confirmed in streptozotocin diabetic. [35], in contrast, Meral et al, 2001indicated that the anti-hyperglycaemic effect of N. sativa is independent of its insulinotropic action [36].

However, the hepatic glucose production through gluconeogenesisis known to contribute significantly to Hyperglycaemia in diabetic patients [37]. Studies on isolated hepatocytes demonstrated a significant decrease in glucose output from gluconeogenic precursors (alanine,glycerol and lactate) in N. sativa oil treated compared to untreated animals [38, 39]. This significant decrease in liver glucose output suggests that the observed antidiabetic action of N. sativa oil is at leastpartially mediated through a decrease in hepatic gluconeogenesis through the inhibition of the enzymatic activities of phosphoenol pyruvate carboxykinase(PEPCK) and of pyruvate carboxylase (PC) [38]. Increased glycolysis in peripheral tissues and/or inhibition of the release of counter-regulatory hormones (e.g., glucagon, cortisol and growth hormone)are possible contributory mechanisms that may be considered and require further investigation [39].

4. Conclusion

From this study we can conclude that crude natural herbs contain several hundred constituents and some of them are present at very low concentrations each one may have benefits or no effect. Commercial products may use only the major constituents; some of them are composed from volatile oil. During formulation process or long standing storage may lose their activity. In our study commercial NS capsules showed significant elevation in fasting blood sugar with no effect on other parameters. Further study should be focused on the efficacy of commercial products after their storage through quality control assessment.

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