Original Article

Effect of Nigella Sativa (Kalonji) on Serum Lipid Profile

Saghir Akhtar Ali,[1] **Fareeha Asghar,**[2] **Mohammad Nafees,**[3] **M. Tayyab**[4]

Abstract

The seeds of Nigella Sativa (Kalonji) have been used as a natural remedy to treat many diseases, including hyperlipidemia. The aim of this study was to examine the hypolipidemic and hypochlesterolemic effects of kalonji in albino rats. Eighty Four (84) albino rats were divided into 6 groups control (C) and experimental (E). The diet contained palm oil in increasing concentrations with one group having added atherogenic supplement. Kalonji was added as 5 ml / kg body weight in powdered form. At the end of the study, the serum levels of total cholesterol, triglycerides and LDL-c were found to be significantly low ($P < 0.05$). Hence, these findings demonstrate that Nigella Sativa (Kalonji) can favorably decrease serum lipid profile and it may be considered as a useful therapy for hyperlipidemia.

Ali S.A.[1]
Associate Professor Pathology
Mohi-ud-Din Islamic Medical College, Mirpur AJK

Asghar F.[2]
Assistant Professor of Histopathology, SIMS, Lahore

Nafees M.[3]
Associate Professor Pathology, Rashid Latif Medical College, Lahore

Tayyab M.[4]
Professor and Head, Department of Pathology
Mohi-ud-Din Islamic Medical College, Mirpur AJK

Key Words: Kalonji, Oxygen Free Radicals, Thymoquinone.

Introduction

Hyperlipidemia is an important risk factor for cardiovascular disease and a serious public health problem in the world. Its major role in the pathogenesis of atherosclerosis has been implicated by several clinical and epidemiological studies (Jaffar et al, 2004).

Hyperlipidemia also has an indirect role by stimulating the production of oxygen free radicals (OFRs) from polymorphonuclear leukocytes (PMNLs) and monocytes (Prasad et al, 2005). Regarding its treatment, nowadays there is an increasing interest towards the potential health benefits of medicinal plants. *Nigella sativa* Linn also known as black seeds or black cumin, is an annual herb from the botanical family of Ranunculaceae.

The seeds of the plant have been used in Southeast Asia, Middle and Far East as a natural remedy to treat many diseases, including asthma, hypertension, diabetes, hypercholesterolemia, inflammation, arthritis, tumors, gastrointestinal disturbances and gynecological disorders for over 2000 years (Ali and Blunden, 2003; El – Din et al., 2006; Ramadan, 2007).

The seeds of *Nigella sativa* have over 100 different chemical components, including mucilage, crude fiber, reducing sugars, resins, alkaloids, flavonoids, organic acids, sterols, tannins and saponins, in addition to the high content of unsaturated fatty acids, especially linoleic acid and oleic acid and proteins. It is known that the biological activity of *Nigella sativa*

seeds is attributed to their essential oil components (Hajhashemi et al., 2004). The main compounds contained are thymoquinone (30 – 48%), p-cymene (7 – 15%), carvacrol (6 – 12%), 4 – terpineol (2 – 7%), tanethole (1 – 4%) and a sesquiterpene longifolene (1 – 8%) (Burits and Bucar, 2000) in which thymoquinone (TQ) and its derivatives [dithymoquinone (DTQ), thymohydroquinone (THQ) and thymol (THY)] are the most putative pharmacologically active constituents of Nigella *sativa* (Padhye et al, 2008).

The side effects Nigella *sativa* have been shown that there were no toxic effects when its oil was given to mice via stomach; it has also been reported that Nigella seed powder does not produce any toxic effect when given to rabbits by gastric intubation (Akhondian et al, 2007). Moreover in another study the low toxicity of *Nigella sativa* fixed oil evidenced by high LD_{50} values, key hepatic enzyme stability and organ integrity, suggested a wide margin of safety for therapeutic doses of its fixed oil (Zaoui et al., 2002).

Materials and Methods

Eighty four (84) Albino rats, with equal number of males and females, weighing 100 – 150 gm were selected for the study. Their ages at the start of the study were 8 weeks. They were divided into six groups. Each group was numbered. Males and females were kept in separate cages in the animal house of Postgraduate Medical Institute Lahore. At the start of study the animals were weighed and grouped according to different diets (Table 1). The diets were started at zero weeks and continued for 12 weeks. Optimum temperature and hygienic conditions were maintained.

Table 1: Animals Grouping Based on Diets.

Groups	No. of Animals	Sex		Type of Diet Given
		Male	Female	
C_1	14	7	7	A
E_1	14	7	7	B
C_2	14	7	7	C
E_2	14	7	7	D
C_3	14	7	7	E
E_3	14	7	7	F

Experimental Diets

Six different diets were prepared. These included normal fat control diets (A and B) and four high fat diets (C to F), (Table 2). The control diet A contained 2.9% palm oil and diet B contained 2.9% palm oil with kalonji. The diet C contained 20% palm oil, diet D included 20% palm oil with powdered kalonji. Diet E contained 20% palm oil with antithyroid drug (Propyl Thiouracil) and bile salts. (Sodium taurocholate and sodium glycocholate).

Table 2: Composition of Diets.

S. No.	Ingredients (gm / 100 gm)	Diets					
		A	B	C	D	E	F
1.	Wheat starch	62.1	62.1	45	45	44.6	44.6
2.	Casein	20.0	20.0	20.0	20.0	20.0	20.0
3.	Glucose	10.0	10.0	10.0	10.0	10.0	10.0
4.	Choline / Methionine	0.5	0.5	0.5	0.5	0.5	0.5
5.	Mineral mixture	3.5	3.5	3.5	3.5	3.5	3.5
6.	Vitamin mixture	1.0	1.0	1.0	1.0	1.0	1.0
7.	Palm Oil	2.9	2.9	2.9	2.9	2.9	2.9
8.	Bile salt	-	-	-	-	0.3	0.3
9.	Prophylthiouracil	-	-	-	-	0.1	0.1
10.	Kalonji (30 mg / kg body wt.)	-	+	-	+	-	+

Methodology

Estimation of total lipids (Gradwohl, 1980).

Estimation of serum total cholesterol (Stein and Mager, 1994).

Estimation of serum triglycerides (Stein and Mayer, 1994).

Estimation of serum HDL – c (Richwond 1973).

Estimation of serum LDL – c (Friedxwal et al 1972).

Statistical Analysis

Results are expressed as mean ± SD.

Statistical analysis was performed on SPSS software (version 14) using unpaired Student's t-test, to compare results between two groups in different times. Moreover comparison within each group (before-after test was conducted using paired Student's t test. P-values less than 0.05 were considered statistically significant.

Results

The sequential changes in serum TC, TG, LDLc, HDLc, TC / HDLc and LDLc / HDLc are summarized in the following tables:

High cholesterol diet significantly increased the level of serum lipid profile compared to baseline ($p< 0.001$). There was no statistically significant difference

Table 3: Comparison of Serum Triglycerdes between Various Groups of Albino Rat at 0, 6, and 12 Weeks (Results are given in mg/dl as mean ± SD).

Groups	0 Week	6 Weeks	12 Weeks
C_1	115.25 ± 4.87	117.8 ± 7.23	123.46 ± 6.72
E_1	112.65 ± 5.68	108.46 ± 8.82	119.17 ± 5.65
C_2	114.35 ± 5.56	120.4 ± 3.31	127.56 ± 8.08
E_2	115.05 ± 6.85	124.88 ± 9.7	132.17 ± 6.99
C_3	112.85 ± 6.74	120.96 ± 7.22	126.35 ± 5.7
E_3	114.58 ± 6.13	112.25 ± 9.12	118.96 ± 5.2

Table 4: Comparison of Serum LDL-c between Various Groups of Albino Rat at 0, 6, and 12 Weeks (Results are given in mg/dl as mean ± SD).

Groups	0 week	6 weeks	12 weeks
C_1	9.04 ± 3.90	14.05 ± 6.76	15.30 ± 10.32
E_1	13.10 ± 6.77	5.36 ± 2.97	11.63 ± 6.96
C_2	13.46 ± 5.35	22.10 ± 8.31	10.86 ± 5.46
E_2	12.58 ± 5.86	5.37 ± 3.58	5.67 ± 2.55
C_3	16.41 ± 5.29	9.47 ± 6.93	23.24 ± 9.18
E_3	13.45 ± 6.86	7.94 ± 1.94	30.09 ± 8.86

Table 5: Comparison of Serum HDL-c between Various Groups of Albino Rat at 0, 6, and 12 Weeks (Results are given in mg/dl as mean ± SD).

Groups	0 week	6 weeks	12 weeks
C_1	45.42 ± 5.37	69.49 ± 4.21	75.85 ± 6.99
E_1	41.92 ± 4.79	72.7 ± 8.08	77.11 ± 4.94
C_2	40.91 ± 3.87	66.31 ± 4.91	83.02 ± 4.67
E_2	41.15 ± 4.02	77.96 ± 4.39	84.88 ± 5.25
C_3	40.84 ± 3.84	79.14 ± 5.98	81.85 ± 2.86
E_3	41.17 ± 3.66	79.79 ± 5.6	83.75 ± 4.06

in serum lipid profile between groups at baseline and after induction. After 3 months of treatment with kalonji, the concentrations of serum TC, LDL-c, HDL-c, TG and TC / HDL-c were significantly lower in treatment group as compared to control group.

Discussion

Enriched fatty diets are usually associated with elevated plasma cholesterol and beta lipoprotein concentration which contribute to the development of atherosclerosis (Apgar et al, 1987, Grundy et al, 1987). Recently sub-fractions of cholesterol i.e. LDL-c and HDL-c have been studied as important associates of CHD (Khan et al 1991, Zock et al 1992). LDLc are involved in the formation of atherosclerotic lesions, particularly after their unsaturated fatty acid have become oxidized, (Esterbauer et al 1989, Serbinovaetal 1992).

Saturated fats and cholesterol fed albino rats had increased LDL-c lipid fractions contributing to coronary heart disease (Tayyab et al 1991, Sahito et al 1993).

The results of the present study showed significant decrease in the development of hyperlipidemia in kalonji group as serum lipid profile were significantly lower as compared to control group (Table 4).

This study with inter-comparison of Nigella sativa containing diets revealed that total cholesterol and LDL-c were decreased and the decrease was statistically significant. HDL-c was increased. The decrease in serum total cholesterol and LDL-c in the E_l and E_2 groups show the cholerectic activity of nigella sativa also reported by El-Dhakhany 1982 (Table 3).

In combination with palm oil, nigella sativa further lowers LDL-c levels, as palm oil contains tocotrienols, which inhibits the biosynthesis of LDL-c, already reported by Qureshi et al 1986 and Qureshi et al 1991. So a diet which is a mixture of palm oil and Nigella sativa proves to be antiatherogenic.

A significant reduction was observed in serum TC and LDL-c of patients with mild hypertension after 8 weeks of black seed extract oral administration (Dehkordi and Kamkhah, 2008). The results of Bamosa et al. (2002) demonstrated a decrease in serum TC, LDL-c, HDL-c and TG during intraperitonial injection of thymoquinone in rats.

Mechanism of hypolipidemic action of TQ is not fully understood; however, decreased cholesterol synthesis and more importantly, its antioxidant role has been proposed. Lipid lowering effects of dietary soluble fibers (Brown et al., 1999; Talati et al., 2009 Moruisi et al, 2006) are probably related to decreased dietary cholesterol absorption, increased primary bile acid synthesis and its fecal loss.

Summary

In conclusion, dietary supplementation with crushed kalonji seed favorably decreased serum lipid profile levels in hyperlipidemic rats; therefore, it may be regarded as a useful therapy for hyperlipidemia. However, further studies are required to study its effects on hyperlipidemic patients and compare it with lipid lowering drugs.

References

1. AH BH, Blunden G. Pharmacological and toxicological properties of nigella sativa. Phytother. Res. 2003; 17 (4): 299-305.
2. Akhondian J, Parsa A, Rakhshande H. The effect of nigella sativa L. (black cumin seed) on intractable pediatric seizures Med. Sci. Monit. 2007; 13: 555-9.
3. Apgar JL, Shevelly CA, Tarka SM. Digestibilityof coca butter and corn oil and their influence on fatty acid distribution in rats. J Nutr 1987;117:660-65
4. Arts 1C, Hollman PC. Polyphenols and disease risk in epidemiologic studies. Am. J. Clin. Nutr. 2005; 81: 317S-325S.
5. Brown L, Rosner B. Willett WW, Sacks FM. Cholesterol – lowering effects of dietary fiber: a meta – analysis. Am. J. Clin. Nutr. 1999; 69 (1): 30.
6. Burits M, Bucar F. Antioxidant activity of Nigella sativa essential jeTil. Phytother. Res. 2000; 14 (5): 323-8.
7. Dehkordi FR, Kamkhah AF. Antihypertensive effect of Nigella sativa seed extract in patients with mild hypertension. Fundam. Clin. Pharmacol 2008; 22 (4): 447-52.
8. EL-Dakhakhany M. Some pharmacological properties of some constituents of nigella sativa seeds: The carbonyl fraction of essential oil. Proceedings of the 2nd International concerence on Islamic Medicine Kuwait, 1982: 426-31.
9. El-Din K, El-Tahir H, Bakeet DM. The black seed (Nigella sativa Linnaeus) – a mine for multi cures: A plea for urgent clinical evaluation of its volatile oil. JTU. Med. Sci. 2006; 1: 1-19.
10. Esterbauer H, Rotheneder M, Striegl G et al. Vitamin E and other lipophilic antioxidants protect LDL against oxidation. Fat Sci Technol 1989; 91: 316-24.
11. Gilani AH, Jabeen O, Asad Ullah Khan M. A review of medicinal uses and pharmacological activities of Nigella sativa. Pak. J. Biol. Sci. 2004; 7 (4): 441-451.

12. Grundy SM. Monounsaturated fatty acid, plasma cholesterol and coronary heart disease. Am J Clin Nutr 1987; 45: 1167-75.
13. Jaffar AR, Babb J, Movahed A. Optimal management of hyperlipidemia in primary prevention of cardiovascular disease. Int. J. Cardiol. 2004; 97 (3): 355-366.
14. Kaleem M, Kirmani D, Asif M, Ahmed Q, Bano B. Biochemical effects of Nigella sativa L seeds in diabetic rats. Indian. J. Exp. Biol. 2006; 44 (9): 745-8.
15. Khan SA, Chughtai AB, Khalid L, Jaffery SA. Comparative physiological evaluation of palm oil and hydrogenated vegetable oils in Pakistan. Proceedings PORIM International Palm Oil Development Conference, Module: Nutrition and Health Aspects of Palm Oil, Kuala Lampur. 1991: 16-20.
16. Le PM, Benhaddou – Andaloussi A, Elimadi A, Settaf A, Cherrah Y, Haddad PS. The petroleum ether exract of nigella sative exerts lipid – lowering and insulin – sensitizing actions in the rat. J Ehnopharmacol, 2004; 94: 251-9.
17. Moruisi KG, Oosthuizen W, Opperman AM. Phytosterols / stanols lower cholesterol concentrations in familial hypercholesterolemic subjects: a systematic review with meta – analyses. J. Am. Coll. Nutr. 2006; 25 (1): 41-8.
18. Padhye S, Banerjee S, Ahmad A, Mohammad R, Sarkar FH. From here to eternity – the secret of Pharaohs: Therapeutic potential of black cumin seeds and beyond. Cancer. Ther. 2008; 6 (b): 495-510.
19. Pburghassem – Gargari et al. 821 Hajhashemi V, Ghannadi A, Jafarabadi H. Black cumin seed essential oil, as a potent analgesic and anti-inflammatory drug. Phytother. Res. 2004; 18 (3): 195-199.
20. Prasad K. Hypocholesterolemic and anti-atherosclerotic effect of flax lignan complex isolated from flaxseed. Atherosclerosis. 2005; 179 (2): 169-275.
21. Qureshi AA, et al. The structure of an inhibitor of cholesterol biosynthesis isolated from barley. J Biol Chem 1986; 261: 10544-50.
22. Qureshi AA, Qureshi NZ, Shen G, Kramer A, Gapor AB, et al. Lowering of serum cholesterol in hypercholesterolemic humans by tocotrienols (palm vit e.) Am J Clin Nutr 1991; 53: 1021S-26S.
23. Ramadan MF. Nutritional value, functional properties and nutraceutical applications of black cumin (Nigella sativa L.): an overview. Int. J. Food. Sci. Tech. 2007; 42 (10): 1208-1218.
24. Sahito MM. Effects of long term administration of various dietary fats on serum and tissue lipids in the rat. (Thesis) Lahore: University of the Punjab, 1993: 239-42.
25. Serbinova ES, Khwaja J, CatdiocJ, et al. Palm Oil Vitamin E protects against ischaemia / reperfusion injury in the isolated perfused langendorf heart. Nutr Res 1992; 12: S203-S15.
26. Talati R, Baker WL, Pabilonia MS. White CM, Coleman Cl. The effects of barley-derived soluble fiber on serum lipids. Ann. Fam Phvtother. Res. 2009; 18 (3): 195-199.
27. Tayyab M, Shad MA, Khan H, Chaudhry NA. Effects of dietary lipids on serum lipid profile. Proceedings Third International Conference. Pak J Pathol 1991; 109: 55-56.
28. Zock PL and Katan MB Hydrogenation alternatives: Effects of trans fatty acids and stearic acid versus linoleic acid on serum lipids and lipoproteins in humans. J Lipid Res 1992; 33: 399-410