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Hypolipidemic and Hypocholestrolemic Effect of Medicinal Plant Combination in the Diet of Rats: Black Cumin Seed (*Nigella sativa*) and Turmeric (Curcumin)

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Abstract: A total of 24 rats were fed a diet either without (Group1) or with black cumin seed 2% (Group 2) or turmeric 2% (Group 3) or plant combination (1% each; Group 4) for 6 weeks. Body weight, feed intake and feed conversion ratio were recorded. At the end of the experiment, blood samples were collected from all groups. The whole blood and harvested sera were used for determination of hematological and biochemical parameters, respectively. The body weight gain and feed conversation ratio were comparable in all treated group when compared with the control. The Packed Cell Volume (PCV), Hemoglobin percentage (Hb%) and Mean Corpuscular Hemoglobin Concentration (MCHC) remained unchanged in all treated group when compared with the control. Spectrophotometric analysis revealed that serum total protein was significantly ($p<0.05$) higher in black seed (Group 2) and turmeric (Group 3) treated groups when compared with the control. Globulin value was significantly ($p<0.05$) higher in black cumin seed treated group than those of control and other groups. The hypolipidemic effect was recorded only in rats fed combination of medicinal plants. The hypocholestrolemia accompanied by lower level of Low Density Lipoprotein cholesterol (LDL-c) was recorded in rats fed both medicinal plants either alone or in combination. However, this effect was more pronounced in rats fed plants combination. The values of albumin, Alanine Transaminase (ALT), Aspartate Transaminase (AST), High Density Lipoprotein cholesterol (HDL-c), Very Low Density Lipoprotein cholesterol (VLDL-c), uric acid and creatinine in all treated groups remained comparable to those of the control group. The present study concluded that plant combination was safe to the animals as reflected on unchanged liver and kidney function biomarkers. Interestingly, black cumin seed and turmeric has hypocholesterolemic effect whenever administered alone or in combination (1% each) whereas the hypolipidemic effect was related to the combined administration of both plants only in the diet of rats.

Key words: Medicinal plants, blood, serum, lipid profile, biochemical parameters, rats

INTRODUCTION

Hyperlipidemia being an important risk factor for cardiovascular disease is 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). Regarding its treatment, now a days there is an increasing interest toward the potential health benefits of medicinal plants.

Black cumin seed (*Nigella sativa*) is a herbaceous plant which is a member of the Ranunculocea family. The seed contains >30% fixed oil and about 0.45% (w/w) of volatile oils (Abd El-Aal and Attia 1993; El-Dakhakhny *et al*., 2000). The black cumin seed has antibacterial and antifungal properties (Rathee *et al*., 1982; Gilani *et al*., 2004; Hasan *et al*., 2005; Abu-Al-Basal, 2011), anthelmintic activity against tape worms (Agarwal *et al*., 1979) and choleretic action (Mahfouz *et al*., 1962) and anticarcinogenic (Aggarwal *et al*., 2005). Injection of black cumin seed extract to male rats (0.4 mL kg^{-1} of body weight) decreased cholesterol levels but it increased the total serum protein and globulins levels meanwhile the values of serum albumin and urea were not significantly altered (Hedaya, 1995). Black cumin seeds have been reported to posses a favorable effect on serum lipid profile by decreasing the levels of total cholesterol, LDL-c, TAG and by elevating the HDL-c levels in rats (Badari *et al*., 2000; Bashandy, 1996; Chaudary, 1996; El-Dakhakhny *et al*., 2000; Hassanin and Hassan, 1996; Tayyab, 1995; Alsaif, 2008).

Turmeric (*Curcuma longa*) is a perennial herb that grows to a height of three to five feet and is cultivated

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extensively in Asia and other countries with a tropical climate. Turmeric is a member of the Curcuma botanical group which is part of the ginger family of herbs, Zingiberaceae. Curcumin, the active ingredient from the spice turmeric is a potent antioxidant (El-Bahr *et al*., 2007; Salama and El-Bahr, 2007; Sivabalan and Anuradha, 2010; Mehta *et al*., 2012) and hepatoprotective properties (Pal *et al*., 2001). The root and rhizome (underground stem) of the *Curcuma longa* L. plant is crushed and powdered into ground turmeric. Turmeric has hypocholesterolemic effect on hypercholesterolemic rats and decreased the raised level of liver cholesterol of cholesterol-fed rats (Reddy and Lokesh, 1994). The combined administration of Turmeric and black cumin seed was examined only in mugil cephalus fish (El-Bahr and Saad, 2008). Therefore, the present study aimed to investigate the effect of combined administration of black cumin seed and turmeric on some biochemical parameters with special references to lipid profiles in rats.

MATERIALS AND METHODS

Experimental animals: A total of twenty four adult albino rats weighing between 193±7 g (8 weeks age at the start) were obtained from the laboratory animal house of the College of Veterinary Medicine, King Faisal University, Saudi Arabia. They were maintained as performed by national guidelines and protocols, approved by the University Animal Ethics Committee. They were housed in clean and disinfected plastic cages. Commercial basal diet and water were provided *ad libitum*. Rats were subjected to natural photoperiod of 12 h light: dark cycle throughout the experimental period (6 weeks). All rats received basal diet for 2 weeks before the start of the experiment for adaptation and to ensure normal growth and behavior. They were maintained in their respective groups for 42 days, monitored closely every day and weighed every week. The rat food was weighed every day before and after feeding the animals to determine the daily food intake.

Plant materials: Turmeric (*curcuma longa*) and black cumin seed (*Nigella sativa*) were purchased from a local market in Al-Ahsa, Saudi Arabia and identified by botanists in the Faculty of Agriculture, King Faisal University, Saudi Arabia. Both plants were analyzed and their ingredients are shown in Table 1 (AOAC, 1995). The whole black cumin seeds and Turmeric were crushed in a blender and mixed with the diet (20 g kg^{-1} diet; 2%) while plant combination was used to obtain (10 g kg^{-1} diet; 1% for each plant).

Table 1: Proximate analysis of ingredients used in the diets of the experiment, dry matter basis

	Percentage					
Ingredients	Moisture	CP	EE	CF	NFE*	Ash
Black cumin seed	5.8	19.54	34.4	6.1	36.16	3.80
Turmeric	13.5	11.74	6.4	7.2	70.07	4.59

CP: Crude Protein; EE: Ether Extract; CF: Crude Fiber and *NFE: Nitrogen Free Extract is calculated by differences

Experimental design and sampling analysis: The rats were divided into five groups (6 rats each).

- Group 1: Rats fed basal diet (control rats)
- Group 2: Black cumin seed treated rats
- Group 3: Turmeric treated rats
- Group 4: Black cumin seed and turmeric plant combination treated rats

Daily measurements of body weight and food intake were recorded. Body weight, feed intake and feed conversion were determined at the start and at the end of the experiment (after 6 weeks). At the end of the experiment, blood samples were collected with and without anticoagulant for whole blood and serum analysis, respectively. Packed Cell Volume (PCV) was measured by a standard manual technique using microhematocrit capillary tubes and centrifuged at 2500 rpm for 5 min measurement of hemoglobin was performed using hemometer. Serum was separated by centrifugation for 10 min at 1200 g and was immediately frozen at -20°C until the time of analysis. The sera were used for spectrophotometric determination of the activities of Aspartate Transaminase (AST) and Alanine Transaminase (ALT) as directed by Reitman and Frankel (1957). In addition, total protein, albumin and globulin values were determined spectrophotometrically as implied by the methods of Doumas *et al*. (1981) and Reinhold (1953), respectively. Serum uric acid and creatinine were determined according to the method described by Tabacco *et al*. (1979). Furthermore, the obtained sera were used for spectrophotometric analysis of serum Triacylglycerol (TAG), total cholesterol by using of enzymatic method of commercial kits according to the methods of Gottfried and Rosenberg (1973) and Zak *et al*. (1954), respectively. Very Low Density Lipoprotein cholesterol (VLDL-c) was calculated by division of TAG by 5 while the LDL-c was calculated as total cholesterol (HDL-c + VLDL-c) = mg dL^{-1} (Bauer, 1982).

Statistical analysis: All the grouped data were statistically evaluated and the significance of changes caused by various treatments was determined using Students t-test (Chou, 1975). The results have been

expressed as means±SD from seven rats in each group. A two ways ANOVA was also done wherever appropriate. The level of statistical significance was set at $p<0.05$.

RESULTS AND DISCUSSION

Performance data: The present study showed that there was no significant changes ($p<0.05$) in weight gain in all treated group when compared with the control (Table 2). The data shown in Table 3 demonstrated that feed intake was significantly higher ($p<0.05$) in all treated group when compared with the control without any significant difference ($p<0.05$) in feed conversion ratio. The increase in feed intake was more pronounced in rats fed plant combination (Group 4) than other treated groups (Group 2 and 3).

Hematological and biochemical parameters: Hematological findings (Table 4) indicated that PCV, Hb and MCHC were remained unchanged significantly ($p<0.05$) in all treated group when compared with the control.

Table 2: Effect of oral administration of turmeric and/or black cumin seed for 6 weeks on body weight gain (g)

	Body weight (g)		
Groups	Initial	6th week	Gain in body weight (g)
I	228±5.1	262±6.2	34
II	228±7.2	258±7.1	30
III	230±4.2	260±3.1	30
IV	236±5.2	266±8.1	30

I (control), II (black cumin seed treated group), III (turmeric treated group), IV (black cumin seed and turmeric treated group) and values are mean±SD of 6 rats

Table 3: Effect of oral administration of turmeric and/or black cumin seed for 6 weeks on food intake (g day^{-1}) and feed conversion ratio (g diet/g weight) in rats

	Food intake (g day^{-1})		Food conversion ratio	
Groups	1st week	6th week	1st week	6th week
I	25.5±0.1	23.0±0.1	0.11±0.1	0.09±0.01
II	27.0±0.2*	26.2±0.5*	0.12±0.1	0.10±0.01
III	30.1±0.1*	25.0±0.6*	0.13±0.1	0.10±0.02
IV	31.2±0.2**	30.0±0.1**	0.13±0.1	0.11±0.01

I (control), II (black cumin seed treated group), III (turmeric treated group), IV (black cumin seed and turmeric treated group), values are mean±SD of 6 rats; *Means within the same column are statistically significant when compared to control (Group I) at $p<0.05$; ** Means within the same column are statistically significant when compared to other group at $p<0.05$

Table 4: Effect of oral administration of turmeric and/or black cumin seed for 6 weeks on hematological parameters in rats

Parameters (%)	I	II	III	IV
PCV	41.1±0.11	41.2±0.12	42.3±0.60	42.3±0.60
Hb	13.2±0.30	12.9±0.70	13.6±0.60	12.6±0.80
MCHC	32.1±1.22	31.3±0.91	32.1±0.10	29.81±0.1

I (control), II (black cumin seed treated group), III (turmeric treated group), IV (black cumin seed and turmeric treated group) and values are mean±SD of 6 rats

Serum total protein level was significantly ($p<0.05$) higher in black seed (Group 2) and turmeric (Group 3) treated groups when compared with the control (Group 4). In addition, globulin value was significantly ($p<0.05$) higher in black cumin seed treated group than those of the control and other groups (Group 4). Albumin, ALT, AST, HDL-c, VLDL-c, uric acid and creatinine levels were unchanged significantly ($p<0.05$) in all treated group when compared with the control (Group 4). Spectrophotometric analysis revealed a significant ($p<0.05$) lower levels of TAG in rats received plant combination (Group 4) when compared with the control whereas the level of this parameter was comparable to the control in other treated groups ($p<0.05$). The present findings showed a significant ($p<0.05$) lower levels of total cholesterol and LDL-c in rats received both medicinal plants either alone or in combination when compared with the control. However, the decrease in total cholesterol and LDL-c was more pronounced ($p<0.05$) in rats received plant combination (Table 4).

Although, some publications have described different beneficial properties of black cumin seed as its extract, oil or active compound (s) such as thymoquinone, to date few have examined the effects of whole or crushed seed (Ibraheim, 2002; El-Bahr, 2007; Buriro and Tayyab, 2007; Pourghassem-Gargari *et al*., 2009; Nasir and Grashorn, 2010; Tasawar *et al*., 2011). In the contrary, many research articles demonstrated the beneficial effect of turmeric (Soliman, 2005; El-Bahr *et al*., 2007; Salama and El-Bahr, 2007; Basavaraj *et al*., 2011; Nouzarian *et al*., 2011). To the researcher knowledge, the present study is the first study demonstrated the effect of combined administration of these medicinal plants on lipid profiles or rats serum. However, El-Bahr and Saad (2008) demonstrated the positive effect of combined administration of black cumin seed and turmeric in *Mugil cephalus* fish.

The data concerning the effect of black cumin seed or turmeric in different animal species was contradicted. In the present study, blood hematology picture, PCV, Hb and MCHC did not show significance difference between all treated groups when compared with the control. Similar results demonstrated that neither turmeric (Emadi *et al*., 2007; Basavaraj *et al*., 2011) nor black cumin seed (El-Bagir *et al*., 2010) changed the hematological picture in animal and birds. In the other hand, some studies demonstrated that turmeric increased PCV and hemoglobin percentage (Sugiharto *et al*., 2011) while other studies (Ekanem and Yusuf, 2008) reported a significant elevation of hematological parameters in rat fed lack cumin seed.

The present findings indicated that albumin, ALT, AST, HDL-c, VLDL-c, uric acid and creatinine were not affected by dietary inclusion of black cumin seed and/or turmeric powder in all treated rats when compared with the control. This indicated that both medicinal plants at the examined dose were safe to be included in rat diet as reflected on the above unchanged liver and kidney function biomarkers. In consistence of the results, El-Bagir *et al*. (2010) reported that inclusion of 15% black cumin seed in the diet of rats did not affect the concentration of albumin and globulins. In addition, Ekanem and Yusuf (2008) showed significant increase in serum liver enzyme activities in rats fed black seed oil. Moreover, Shewita and Taha (2011) demonstrated higher ALT and lower AST level in broiler chick fed black cumin seed. Also, Basavaraj *et al*. (2011) supplementation of Turmeric to broiler rabbits did not show significant changes in all above mentioned biochemical parameters (Table 5).

The previously reported hypolipidemic effect of Black cumin seed (Pourghassem-Gargari *et al*., 2009; El-Bagir *et al*., 2010) and turmeric (Hussain, 2002; Srinivasan, 2005; Soliman, 2005; Sugiharto *et al*., 2011) was not similar to the findings. Similar hypolipidemic effect was observed in the present study only when both plants administered together as a combination. This might be indicated that half dose of each plant is enough to induce the hypolipidemic effect.

Cholesterol is transported via blood by lipoproteins. HDL-c (good cholesterol) transports it from tissues to liver and LDL-c (bad cholesterol) does it in the opposite direction. Therefore, decrease in serum LDL-c cholesterol is an indication of low rate of transportation of cholesterol from liver to tissues and subsequent transformation of cholesterol into bile acid by liver enzymes. HDL-c/LDL-c ratio consider as one of the most important parameters in lipid metabolism. It gives an indication as to whether cholesterol is likely to be deposited in the arteries or not (Genest *et al*., 1999). A ratio with lowered LDL-c as noticed in the present study considered beneficial as protecting from atherosclerosis. The hypocholesterolemia showed in the present study in rats treated with black cumin seed was in consistent with other findings in rats (Zaoui *et al*., 2002; El-Dakhakhny *et al*., 2000; Bamosa *et al*., 1997; Kocyigit *et al*., 2009), human (Dehkordi and Kamkhah, 2008) layers (Akhtar *et al*., 2003) and rabbits (Nader *et al*., 2010; Tousson *et al*., 2011). In addition, the hypocholesterolemia showed in the present study in rats treated with turmeric was in accordance with other findings in rats (Hussain, 2002; Soliman, 2005; Kim and Kim, 2010). The pronounced hypocholesterolemia reported in the present study in rats administered the medicinal plant combination was not reported before. The hypocholesterolemia showed in the present study in rats treated with black cumin seed and/or turmeric might be attributed to the control of the microsomal 7α-hydroxylation (the rate limiting enzyme in cholesterol catabolism). The pronounced effect of plant combination on cholesterol metabolism might be resulted from a synergistic effect between active ingredients of both plants. The hypolipidemic and hypocholestrolemic effect of both plants are probably related to decreased dietary cholesterol absorption increased primary bile acid synthesis and its fecal losses. This can be done also by the active ingredient of each plant which may act by making liver cells more efficient to remove LDL-C from blood through increasing LDL receptor densities in liver and by binding to apolipoprotein B (El-Beshbishy *et al*., 2006; Weggemans and Trautwein, 2003).

Table 5: Effect of oral administration of turmeric and/or black cumin seed for 6 weeks on blood biochemistry in rats

Blood biochemistry	Group I	Group II	Group III	Group IV
Total protein (g L^{-1})	6.8±0.4	7.9±0.3*	7.4±0.1*	6.7±0.2
Albumin (g L^{-1})	3.1±0.2	3.3±0.3	3.5±0.1	3.0±0.2
Globulin (g L^{-1})	3.7±0.2	4.6±0.2*	3.9±0.2	3.7±0.2
A/G ratio	0.8±0.2	0.7±0.2	0.9±0.2	0.8±0.2
TAG (mg dL^{-1})	106.4±6.2	104.9±6.2	102.3±4.2	85.6±4.2*
ALT (U L^{-1})	17.9±0.2	18.2±0.2	18.6±0.2	19.1±0.2
AST (U L^{-1})	102.0±1.1	99.0±1.2	101.0±1.1	100.0±1.3
Total colesterol (mg dL^{-1})	179.6±1.2	167.0±1.2*	170.0±2.2*	151.3±4.2**
HDL-c (mg dL^{-1})	54.2±2.9	55.0±3.7	55.0±3.2	57.6±5.6
LDL-c (mg dL^{-1})	104.1±2.1	91.5±1.5*	94.5±2.1*	73.7±0.9**
VLDL-c (mg dL^{-1})	21.3±1.2	21.0±1.2	20.5±1.2	20.0±1.2
Uric acid (mg dL^{-1})	1.2±0.1	1.3±0.1	1.1±0.1	1.1±0.2
Creatinine (mg dL^{-1})	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1

I (control), II (black cumin seed treated group), III (turmeric treated group), IV (black cumin seed and turmeric treated group), values are mean±SD of 6 rats; *Means within the same column are statistically significant when compared to control (Group I) at $p<0.05$; **Means within the same column are statistically significant when compared to other group at $p<0.05$

CONCLUSION

The present study concluded that plant combination was safe to the animals as reflected on unchanged liver and kidney function biomarkers. Black cumin seed and Turmeric has hypocholesterolemic effect whenever administered alone or in combination (1% each) whereas the hypolipidemic effect was related to the combined administration of both plants only in the diet of rats.

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