



CHANGING THE LIPID PROFILE AND RENAL FUNCTIONS BY ALLIUM SATIVUM, NIGELLA SATIVA AND HIBISCUS SABDARIFFA IN ESSENTIAL HYPERTENSIVE PATIENTS

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ABSTRACT

Background: Essential hypertension is a global major health problem affecting more than a billion individual. The aim of the present study is to find out a new effective agent with high safety and low cost by examining Allium sativum, Nigella sativa, and Hibiscus sabdariffa as compared with antihypertensive drug Ramipril. **Materials and Methods:** This study was conducted on 24 hypertensive patients by examining effects of these agents on systolic and diastolic blood pressure in addition to investigating changes in serum lipid profile (cholesterol, triglycerides [HDL and LDL]) and changes in renal functions (serum urea nitrogen, creatinine, uric acid, and electrolytes:

Na⁺, K⁺, and Ca⁺⁺) after administering these agents for 4 weeks. **Results:** There was a significant lowering effect of the four agents on both systolic and diastolic BP. Garlic has shown a significantly elevated HDL while roselle has shown a significantly decreased LDL levels. Other values of lipid are decreased. Moreover, a significant decrease in serum creatinine level with garlic and black seed is seen with a significant decrease of blood urea nitrogen level with roselle. The uric acid and sodium levels are significantly reduced with garlic. **Conclusion:** There is an advantageous effect of using these agents in hypertension therapy.

KEYWORDS: Allium sativum, Nigella sativa, Hibiscus sabdariffa, Hypertension, Lipid profile, Renal functions.

INTRODUCTION

Hypertension is an elevation of either sustained systolic or diastolic arterial blood pressure to 140/90 mmHg respectively or more.^[1] It results from increased vascular smooth muscle tone which leads to increased arterial resistance and reduced capacitance of venous system.^[2] Hypertension is usually mediated by multifactorial causes, but when there is no specific cause can be found, it is said to be an **essential hypertension (EHT)**. It is concerned with ageing, race and genetic factors, stress and emotional factors, environmental and nutritional factors (intake of Na⁺), metabolic syndrome including (obesity, dyslipidemia, diabetes), cardiovascular diseases (C.V.S), smoking, and alcohol consumption.^[3] The arterial blood pressure (BP) is directly proportional to cardiac output (CO) and peripheral vascular resistance (PVR) in that $(BP=CO \times PVR)$.^[4] All antihypertensive drugs act by interfering with the normal physiological mechanisms: postural baroreceptor reflex and renal response to decreased BP via renin-angiotensin and aldosterone system.^[5]

The aim of the present study is to investigate the effect of well-known medicinal herbs: *Allium sativum*, (garlic), *Nigella sativa* (black seed) and *Hibiscus sabdariffa* (roselle) on blood pressure, lipid profile and renal functions in essential hypertension patients.

Garlic (*Allium sativum*) is a perennial plant. Its medicinal parts are the fresh, dried bulb, and oil of garlic. Its constituents are volatile oils, alliin, allicin, ajoene, proteins, amino acids, and prostaglandins.^[6] It has hypolipidemic, hypoglycemic^[7], antithrombotic effect^[8], and antimicrobial effect in salmonellosis.^[9] Black seed contains negillon and negillin glycosides, essential oils, amino acids, and saponin. Black seed is used for the treatment of bronchial asthma.^[10] Moreover, it has antioxidant and antimutagenic effects.^[11] Roselle (*Hibiscus sabdariffa*-L) erect mostly branched annual stem, coloured dark green to red leaves. Flowers contain anthocyanins, betasitosterol, saponins and proteins. Dried calices contain the flavonoid, gossypetin, hibiscetine, sabdarotone, thiamine, riboflavin, and fatty acids.

MATERIALS AND METHODS

Patients: This prospective randomized clinical-case control study was carried out in General Medicine speciality clinic in Al-Kadhimya Teaching Hospital from May 2017 to September 2017. It was approved by ethics committee in Al-Kindy College of Medicine. The study is in accordance with the Helsinki Declaration of 1975 (revised in 2008). Twenty-four patients of both sexes participated in this study 15 females and 9 males. Their ages and weights ranged between (31-65yr) and (65-92kg) respectively. All the patients were complaining

from EHT. A detailed history was taken from each patient. Patients with chronic diseases of liver, kidney, cardiovascular complications, and females who are pregnant or breast feeding are excluded from the study. The selected patients had been informed about the procedure of treatment and a written consent was obtained from each patient. Medications that were used by many patients prior to our study were stopped for 5 days before starting our study. The patients were randomly allocated to four groups (each group contains 6 patients). They were given the followings:

Group 1 (control) received 5 mg ramipril tablet once daily for 4 weeks.

Group 2 received 2.5 garlic tablets (equivalent to 5gm of fresh garlic bulb) in three divided doses with meal daily for four weeks.

Group 3 received 10 *Nigella sativa* oil capsules in two divided doses before meals daily (equal to one gram per day) for 4 weeks.

Group 4 received 15 gram roselle orally as infusion before breakfast for four weeks.

After 12 hours fasting blood samples (7 mls) were collected from all patients by venipuncture for biochemical determination of lipid profile (serum cholesterol, triglycerides, HDL, LDL and VLDL) and that concerning renal functions (serum urea nitrogen, creatinine, uric acid, electrolytes (Na^+ , K^+ , and Ca^+)) by using spectrophotometer methods^[12] and electrolytes analyzer Jokohev-D Japan Roche 9180 US. Blood pressure measured weekly from the beginning of treatment by sphygmomanometer and stethoscope (Planoscope-Germany).

Plants: Garlic was used as a tablet (produced by Nature's Bounty Inc-USA) that contains 400 mg Garlic (bulb) equivalent to 2,000 mg of fresh Garlic bulb. Black seed soft gelatin capsule (produced by Pharco pharmaceutical-Alexandria-Egypt) contains 100 mg black seed oil. The dried leaves of roselle were cleaned carefully and ground by an electrical grinder. Roselle: The calicies were bought from in Baghdad city local market. They were identified by Iraqi National Center of Herbs after removing the foreign materials before starting our study. 15 gm weight of the powder were added to 750 ml of boiling water and let it stand for 10 min. The infusion was given orally by drinking daily calculated quantities for four weeks.^[13] Garlic and black seed doses implemented by manufacturers were used in this study.

Chemicals: All the chemicals used in the present study are of analytical grade. Ramipril (TRITACE®) 5mg tablet was supplied by Aventis Pharma Deutch Land (GMBH) – Germany. The kits for the confirmation of cholesterol, triglycerides, HDL and uric acid were

purchased from Biomerieux – France, and kits for urea creatinine and Ca^{++} was purchased from Randox – UK.

Statistical Analysis: The complete randomized design (CRD) ANOVA procedure within (SAS) 2001 program was used. Less significant difference (LSD) test and Duncan multiple range were used to compare between the means. $P < 0.05$ was considered to be significant.

RESULTS

The obtained results in the present study revealed a significant lowering effect ($*P < 0.01$) of arterial BP (Table 1) in systolic and diastolic EHT in garlic, black seed and roselle (groups 2, 3, and 4) as compared with antihypertensive drug ramipril (group 1). Moreover, comparing the baseline value of the same group with that after 2 and 4 weeks of treatment have shown a significant decline in both systolic and diastolic BP. The results show that roselle was the most potent in decreasing BP followed by garlic then black seed.

The data of table 2 shows a significant increment of HDL in garlic group and decline of LDL in roselle group in comparison with ramipril which significantly reduced cholesterol, HDL and LDL.

Renal function data as presented in **Table 3** shows a significant reduction in serum creatinine of both garlic and black seed ($*P < 0.05$) with a significant lowering effect of uric acid level in garlic group and urea nitrogen in roselle group. At the same time, the levels of Na^+ in garlic and K^+ in black seed were significantly reduced by treatment. By comparing the results of these agents with ramipril, ramipril shows a significant decrease in urea nitrogen level (at $*P < 0.05$), creatinine, uric acid and Ca^{++} levels at $*P < 0.01$.

Table 1: The means of arterial BP levels (systolic and diastolic) mmHg in patients with EHT during four weeks of treatment with ramipril, garlic, black seed, and roselle. **: significant at $P < 0.01$, *: significant at $P < 0.05$. The various letters mean that there was a comparative significant difference between the means of arterial BP levels by Duncan's multiple range test. LSD: least significant difference.

Period	Ramipril		Garlic		Black seed		Roselle	
	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
Baseline	167.14 ±3.23 a	107 ±1.52 a	145 ±7.07a	94 ±4.18 ba	156 ±10.84 a	95 ±3.54 a	162 ±7.58 a	104 ±5.48 a
After one week	152.14 ±6.72 b	94.29 ±3.31b	144.4 ±6.07 a	96 ±2.34 a	150 ±6.12 a	94 ±3 a	144 ±8.94 b	100.6 ±5.64 a
After two week	146.07 ±3.5 c	90.86 ±2.28 c	136 ±8.94 ba	92 ±2.74 b	144 ±4.18 a	92 ±3.53 a	134 ±8.94 c	102.2 ±3.19 a
After three week	144.29 ±3.31 dc	86.79 ±1.97 d	133 ±7.58 bc	86 ±2.24 c	142 ±4.47 ba	90 ±3.54 a	135 ±6.12 cb	90 ±3.54 b
After four week	137.14 ±3.51 d	83.79 ±2.89 b	125 ±7.06 c	84 ±2.23 c	138 ±6.12 b	85 ±5 b	137 ±3.54 c	84 ±4.18 c
L.S.D	9.6**	7.68**	6.4**	3.2**	5.77**	3.21**	8.04**	5.96**

Table 2: The means of serum lipid levels, cholesterol, triglycerides, HDL, LDL, VLDL (mmol/L) in patients with EHT during four weeks of treatment with ramipril, garlic, black seed and roselle. *: significant at $P < 0.05$. Duncan multiple range test. LSD: least significant difference.

Agents	Period	Cholesterol	Triglycerides	HDL	LDL	VLDL
Ramipril	Baseline	5.71±0.51 a	1.94±0.78 a	1.38±0.18 b	3.45±0.58 b	0.88±0.36 a
	After 2 week	5.27±0.41 b	1.98±0.58 a	1.64±0.3 a	2.73±0.45 c	0.9±0.26 a
	After 4 week	5.84±0.61 a	1.96±0.41 a	1.07±0.2 c	3.95±0.4 a	0.89±0.19 a
	L.S.D	0.39 *	0.49	0.18 **	0.37 **	0.21
Garlic	Baseline	5.26±0.46 a	1.65±0.5 a	1.05±0.21 b	3.47±0.52 a	0.75±0.23 a
	After 2 week	5±0.48 a	1.4±0.38 a	1.28±0.16 ba	3.08±0.41 a	0.63±0.18 a
	After 4 week	4.86±0.5 a	1.26±0.35 a	1.41±0.15 a	2.88±0.44 a	0.57±0.16 a
	L.S.D	0.66	0.57	0.24*	0.63	0.26
Black seed	Baseline	5.46±0.29 a	1.7±0.63 a	1.46±0.27 a	3.27±0.23 a	0.77±0.29 a
	After 2 week	5.36±0.28 a	1.57±0.6 a	1.5±0.26 a	3.15±0.22 a	0.71±0.27 a
	After 4 week	5.2±0.29 a	1.3±0.38 a	1.55±0.09 a	3.06±0.28 a	0.59±0.2 a
	L.S.D	0.39	0.75	0.31	0.34	0.34
Roselle	Baseline	4.55±0.18 a	1.48±0.49 a	1.04±0.11 a	2.84±0.26 a	0.67±0.22 a
	After 2 week	4.5±1.2 a	1.8±0.57 a	1.09±0.15 a	2.53±0.41 ba	0.82±0.26 a
	After 4 week	4.3±0.21 a	2±0.59 a	1.2±0.15 a	2.19±0.49 b	0.91±0.27 a
	L.S.D	0.27	0.76	0.2	0.55 *	0.34

Table 3: The means of serum urea nitrogen (mmol/L), creatinine ($\mu\text{mol/L}$), uric acid, Na^+ , K^+ and Ca^{++} (mmol/L) in patients with EHT during four weeks of treatment with ramipril, garlic, black seed and roselle.* :significant at $P<0.05$. Duncan multiple range test. LSD: least significant difference.

Agents	Period	s. urea nitrogen	s. creatinine	s. uric acid	s. Na^+	s. K^+	s. Ca^{++}
Ramipril	Baseline	5.53 ± 0.88 ba	110.43 ± 17.11 a	391.14 ± 9.48 a	140.36 ± 1.51 a	4.63 ± 0.32 a	2.27 ± 0.37 a
	After 2 week	5.1 ± 0.44 b	86.36 ± 20.59 b	268.21 ± 52.36 b	140.64 ± 2.06 a	4.64 ± 0.49 a	2.14 ± 0.37 a
	After 4 week	5.76 ± 0.55 a	102.07 ± 9.54 a	297.71 ± 68.2 b	140.14 ± 1.75 a	4.51 ± 0.33 a	1.64 ± 0.16 a
	L.S.D	0.5 *	12.55 **	38.2 **	1.29	0.29	0.24 **
Garlic	Baseline	3.34 ± 0.57 a	77.5 ± 8.79 a	168.8 ± 5.26 a	143.3 ± 1.3 a	4.4 ± 0.25 a	2.45 ± 0.23 a
	After 2 week	3.32 ± 0.69 a	71 ± 7.97 ba	165.8 ± 4.82 ba	142.4 ± 1.14 ba	4.4 ± 0.12 a	2.6 ± 0.22 a
	After 4 week	3.1 ± 0.52 a	64 ± 5.87 b	159.4 ± 5.64 b	141 ± 1.01 b	4.5 0.16 a	2.5 ± 0.2 a
	L.S.D	0.82	10.53 *	7.24 *	1.59 *	0.26	0.3
Black seed	Baseline	3.7 ± 0.89 a	67.6 ± 4.51 a	228.8 ± 75.59 a	142.06 ± 0.93 a	4.4 ± 0.34 b	2.48 ± 0.25 a
	After 2 week	3.55 ± 0.87 a	65.2 ± 4.15 ba	212.6 ± 72.27 a	141.2 ± 0.84 a	4.4 ± 0.21 b	2.44 ± 0.09 a
	After 4 week	3.4 ± 0.91 a	62.2 ± 2.68 b	201 ± 66.75 a	141 ± 2.65 a	5 ± 0.14 a	2.4 ± 0.13 a
	L.S.D	1.23	5.32 *	98.7	2.33	0.34 **	0.23
Roselle	Baseline	3 ± 0.26 a	84.64 ± 8.16 a	312 ± 66.77 a	140.42 ± 0.58 a	4.06 ± 0.08 a	2.4 ± 0.16 a
	After 2 week	2.84 ± 0.23 ba	83.2 ± 8.87 a	307 ± 59.4 a	140 ± 2.45 a	4.02 ± 0.11 a	2.4 ± 0.12 a
	After 4 week	2.54 ± 0.23 b	80.4 ± 7.3 a	305.6 ± 54.95 a	138 ± 2.45 a	4.02 ± 0.04 a	2.3 ± 0.04 a
	L.S.D	0.33 *	11.2	83.47	2.79	0.12	0.2

DISCUSSION

All the medicinal herbs that were used in the present study i.e. garlic, black seed, and roselle have produced a significant lowering effect to systolic and diastolic arterial BP as compared with the results of antihypertensive drug ramipril which is an angiotensin converting enzyme inhibitor. The results of garlic (group 2) are related to its antioxidant property and free radical scavenging ability^[14] and in having γ -glutamyl cysteines compounds in its composition that inhibits angiotensin converting enzyme in vitro.^[15] Garlic also increases the production and activity of nitric oxide that promotes the relaxation of vascular smooth muscles leading to

arterial BP lowering.^[16] The results of the present study are compatible with the results of others^[17] who stated that garlic can lower elevated BP to a normal level.

The antihypertensive effect of black seed (group 3) may be related to thymoquinone which is the main constituent of the volatile oil that is present in black seed, in addition to its antioxidant properties.^[18] Moreover, the hypotensive effect is related to its diuretic effect. The present results are similar to the results of others.^[19] The antihypertensive effect of roselle (group 4) is related to anthocyanins (abundant flavonoids in roselle) that produce hypotensive mechanisms such as inhibiting angiotensin I and II converting enzymes in addition to their diuretic properties^[20] and through the mediation of endothelium derived nitric oxide CAMP relaxant pathway in vascular smooth muscles.^[21] The results of roselle in the present study are similar to others.^[22] When they used roselle tablet orally for hypertensive rabbits for ten days it acts by increasing the blood flow, decreasing peripheral vascular resistance and lowering blood pressure.

Now it is clear that roselle produces more significant reduction in systolic and diastolic BP as compared with garlic and black seed. The effect of medicinal herbs on lipid profile

Table 2 had shown that garlic (group 2) increased HDL level significantly but also decreased cholesterol, triglycerides, LDL levels. Garlic contains the active substance allicin and ajoene that inhibit HMG-CoA reductase enzyme involved in triglycerides and cholesterol biosynthesis in hepatocytes.^[23] The results of the present study are similar to the results of others^[23] who reported that garlic is not clinically relevant lipid lowering in normo-lipidemic individuals but there was a significant increase in serum HDL level. The black seed (group 3) caused no improvement in most serum lipid profiles in the present study, this may be related to the small doses of the herb or may be related to the short duration of therapy. There is controversy in the results of black seed when compared with other studies. Some reported that lowering lipid profile levels requires 12 weeks or more of using the herb to get a significant effect.^[24] Others^[25] revealed that black seed oil in a dose of 800 mg daily for 4 weeks caused a significant decrease in all lipid parameters. Similar results were obtained by^[26] by using black seed for four weeks of treatment in diabetes induced rabbits. In group 4, roselle produced a significant decrease in LDL levels with minor changes in other parameters of lipid profile. The decrease in LDL levels was compatible with results of others^[27] who found that roselle produces a significant decrease in triglycerides and LDL levels with a significant increase in HDL level and slight increase in cholesterol level after 12 weeks

treatment with roselle. Similar results were obtained by at the same time.^[28] Ramipril caused a significant increase in cholesterol and LDL levels and no change in triglycerides level with a significant decrease in HDL level. In general, all the antihypertensive medicinal herbs may improve the renal outcome then confer some renal protection. Garlic (group-2) reduced significantly creatinine, uric acid and Na levels. This is related to its antioxidant effect and free radical scavenging ability.^[29] Garlic is effective in the management of electrolytes related disorders.^[30] Black seed (group-3) caused a significant decrease in creatinine and K level while other parameters keep within the normal range with a slight decrease in urea nitrogen and uric acid levels. These changes are related to thymoquinone. Roselle (group 4) caused a significant decrease in urea nitrogen with a slight decrease in creatinine and uric acid levels due to the diuretic effect of roselle related to the presence of gossypetin flavonoids, anthocyanin and glycoside hibiscin in its composition.^[13] At the same time, ramipril (group 1) produced a significant change in urea nitrogen, creatinine, uric acid and Ca⁺⁺ levels.

CONCLUSION: Garlic, black seed, and roselle are effective in as antihypertensive agents and they are recommended as a support for essential hypertension.

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