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RESEARCH ARTICLE

ROLE OF BADRANJBOYA (NEPETA HINDOSTANA) IN THE PREVENTION OF ATHEROSCLEROSIS: SINGLE BLIND RANDOMISED CONTROLLED CLINICAL TRIAL

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ABSTRACT

Atherosclerosis is the hardening and narrowing of the arteries and is caused by the slow build-up of plaque inside the walls of arteries. The clinical manifestations of atherosclerosis include myocardial infarction, stroke and sudden cardiac death. The prevalence of the disease is high, and approximately 50% of all deaths globally can be attributed to atherosclerosis. The concept of *Dusumate Dam* in Unani literature has been considered responsible for the development of *Salabate Sharaeen* (atherosclerosis) and *Simane Mufrit* (obesity). A randomized, single-blind, standard controlled clinical trial was conducted in National Institute of Unani Medicine Hospital Bangalore, with the objective of evaluating the efficacy of *Badranjboya (Nepeta hindostana)* as a cardio-protective drug. A total of 30 patients with risks of atherosclerosis were selected randomly and assigned into two groups 20 in test and 10 in control groups. Test group was treated with *Badranjboya* powder, 6 grams twice a day for 2 months whereas control group was treated with Garlic powder, 2 grams powder filled in gelatin capsules and given in to two divided doses for the same duration. The response was evaluated by the assessment of subjective parameters (palpitation, breathlessness, headache and chest pain) and objective parameter (blood pressure, lipid profile, haematocrit value and random blood sugar). The data was tabulated and analyzed by using apropriate statistical tests. Test group showed significant reduction in subjective parameters ($p<0.01$) and objective parameters like blood pressure, MDA concentration, whereas significant increase in HDL level ($p<0.01$) but changes in serum cholesterol, triglyceride, LDL, and haematocrit values were found statistically not significant in both groups**.** The effect of the drug was prominent on vessels wall. The overall improvement in test group was highly remarkable, without any clinically and statistically significant side effects or toxicity. Therefore, it can be concluded that *Badranjboya* has encouraging potential in the prevention of atherosclerosis and it may be combined with other treatment modalities like weight control in obese, physical therapy and dietary modification etc. for optimal results.

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INTRODUCTION

Atherosclerosis (Greek 'athero' = gruel/paste; 'sclerosis' = hardening) is the most common underlying pathologic process leading to cardiovascular morbidity and mortality. It is a slow, complex process characterized by accumulation of lipids and thickening of the inner layer of the arterial wall, which in its earliest form, appears to be present even at the fetal stage, and evolves slowly over decades (Riina Oksjoki, 2006). It may manifest as coronary heart disease (e.g. angina, myocardial infarction, and sudden death), cerebrovascular diseases (e.g. stroke and transient ischaemic attack) or peripheral vascular diseases (e.g. claudication and critical limb ischaemia) (Colledge, 2010). In today's world most deaths are attributable to non communicable diseases (35 million) just over half of these (17 million) are as a result of cardiovascular diseases. Cardiovascular diseases become the first and second leading cause responsible for one third of all deaths (WHO, 2003). It is estimated that there were approximately 29.8 million patients with cardiovascular diseases in India during the year 2003, and about 1.5 million people die of cardiovascular diseases every year (Govt. of India annual report 2006-07). Prevention of atherosclerosis reduces the burden of cardiovascular diseases.

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The main preventive approach should be effective reduction of hypercholesterolemia especially the low density lipoprotein (LDL-C) and elimination of lipids accumulated in the tissues by enhancing the catabolism of lipids and sterols. Use of hypolipidemic drugs and reducing the dietary saturated fat and cholesterol are the corner stone of the management of atherosclerosis (Hardman *et al*., 2001; Park, 2007; Carruthers *et al*., 2000; Steinberg, 2005). For the same reason, several hypolipidemic drugs have been already introduced in the conventional medicine such as HMG-Co A reductase (lovastatin, atorvastatin), Niacin, bile acid sequestrates, gemfibrozil and fenofibrates etc (Carruthers *et al*., 2000; Hardman *et al*., 2001; Katzung, 2007). But the long term use of these drugs has been reported for several adverse effects.

It is being appreciated that traditional system of medicine can offer safe, effective and low cost antiatherogenic drugs. Many Unani drugs have demonstrated positive effects in modifying risk factors for coronary heart diseases (Jenkins *et al*., 2002). In Unani literature the concept of *Dusumate Dam* (hyperlipidemia) has been considered responsible for the development of *Salabate Sharaeen* (atherosclerosis) and *Simane Mufrit* (obesity) (Ibn Nafees; Ibn Nafees; Majoosi, 1889). Furthermore, the *Simane Mufrit* (obesity) has been described by a number of Unani physicians and an association has been mentioned between the *Dusumate Dam* (hyperlipidemia), *Salabate Sharaeen* (thickening of arteries) and *Simane Mufrit* (obesity). The etiological factors, clinical features and complications of *Simane Mufrit* are almost similar to that of hyperlipidemia (Majoosi, 1889; Arzani Akbar, 1890; Razi, 1999; Ibn Sina, 2007; Jurjani, 1903). A number of studies have established that obesity and hyperlipidemia are often associated, (Kumar *et al*., 2004; Guyton, 2000; Kasper *et al*., 2005; McGill, 2002; Lakkae, 2001; Tershakovec, 2002) thus are mainly responsible to initiate the endothelial cell injury, inflammatory changes, foam cell formation and finally the atherosclerosis.

Badranjboya (Nepeta hindostana) is mentioned as *Mufarreh wa Muqawwie Qalb* (cardiotonic) in Unani medical literature since ancient times. Apart from cardiotonic effect it has potential to resolve atheroma of coronary artery disease. *Ibn Sina* had mentioned that this drug simultaneously acts through different mechanisms. As a *Mulattif* (Demulcent) it modifies the deposited fat to remove easily, as a *Mufatteh* (Deobstruent), widens the spaces where the fats are lodged in and as a *Muhallil* (Resolvent/Antiinflammatory) resolve them (Ibn Sina, 2007). Thus the present study was conducted with the objective of evaluating the efficacy of *Badranjboya* as a cardio-protective drug.

METHODOLOGY

The present study was conducted in the department of *Tahaffuzi wa Samaji Tib* at National Institute of Unani Medicine, Bangalore India, from 2012-2013 after approval from Institutional Ethical Committee of National Institute of Unani Medicine, Bangalore. Clinical study was started by enrolling eligible patients into test and control groups by random allocation from OPD of NIUM. Total duration of study was 12 months. The study was designed as a randomized single blind, standard controlled clinical trial. The sample size was 30 patients; 20 in test and 10 in control groups respectively. The treatment period was 60 days. Patients of either sex, aged between 35 to 60 years, patients presenting with complaints of hypertension, asymptomatic hypertension BP: ≥130/85 mmHg were enrolled. Patients with uncontrolled diabetes, hypertension or any terminal medical condition are excluded from the study. They were given the information sheet having details regarding the nature of the study, the drug to be used, method of treatment etc. and asked to for their consent voluntarily. During the selection procedure, complete history taking, general physical and systemic examination was carried out and recorded on a prescribed proforma which was designed according to the objectives of the study. All the patients were interrogated about their chief complaints and duration of suffering in detail specially about palpitation, headache, dizziness, breathlessness, chest pain, fatigue, insomnia, nervousness, dysponea, epistaxis. While taking history, emphasis was given on past history for any organic disease especially cardiovascular diseases and diabetes. Dietary habits, type of diet, smoking habits, pan chewing etc were enquired about in personal history.

Hb%, TLC, DLC, RFT, LFT, Lipid peroxidation test (Malondialdehyde i.e. MDA assessment by Ohkawa *et al* 1979) were done in every case before and after treatment whereas lipid profile, random blood sugar and haematocrit were done on every follow- up of 15 days up to two months. Patients were kept under strict observation and advised to come every 15th day in OPD for the assessment till the completion of study. At every visit, patients were asked about the progression or regression in their symptoms, and subjected to assess the clinical findings. Concomitant treatment was not allowed during the study in both groups. Test drug namely Badranjboya (*Nepeta hindostana)* and control drug Lehsun (*Allium sativum*) were provided by pharmacy of National Institute of Unani Medicine, Bangalore after proper identification of the drug done by chief pharmacist, National Institute of Unani Medicine, to ensure their originality and authenticity. The drugs were cleaned by weeding out unwanted material and impurities then grinded to make fine powder. Test group was treated with 6 gm *Sufoof* (powder) of Badranjboya (*Nepeta hindostana)* orally in the morning and same dose in the evening for two months. Control group was treated with 1 gm powder of Lehsun (*Allium sativum*) filled in gelatin capsules of 500 mg capacity and advised 2 capsules to be taken orally in the morning and evening for the same period of time as that of test drug.

The assessment of the efficacy in the test and control groups was based on objective and subjective parameters. Assessment of objective parameters like blood pressure mesurement, lipid profile, random blood sugar and haematocrit was done on every 15th day while Lipid peroxidation test was done before and after treatment. Subjective parameters included symptom like palpitation, breathlessness, headache and chest pain. As these parameters differ in severity from patient to patient, an arbitrary grading of subjective parameters was improvised for appropriate assessment and statistical evaluation. Before starting treatment, baseline observations were recorded in the case report form and any change in the parameters was noted down at every follow up visit till the end of the treatment. After 60 days of the treatment, values of different parameters were analyzed and compared statistically. These parameters are as follows:

Palpitation (The Criteria Committee for the New York Heart Association, 1994): Palpitation was assessed on 4 point scale ranging from 1-4

grade	
1	No limitation of physical activity. Ordinary physical activity does not cause palpitation.
2	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in palpitation.
3	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes palpitation
4	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

Breathlessness (Michael, 2006): Breathlessness was assessed on 5 point scale ranging from 1-5

grade	
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying or walking up a slight hill
3	Walks slower than a contemporary on level ground because of breathlessness, or has to stop for breath when walking at own place
4	Stops for breath after walking about 100 m or after a few minutes on level ground
5	Too breathless to leave the house, or breathless when dressing or undressing

Headache: Headache was assessed on 4 point scale ranging from 1-4

grade	
0	No pain
1	Mild – headache
2	Moderate –headache
3	Severe –headache

Chest pain: Chest pain was was assessed on 4 point scale ranging from 1-4

grade	
0	No pain
1	Mild - Chest pain
2	Moderate - Chest pain
3	Severe - Chest pain

Statistical analysis Statistical analysis was carried out to analyse the data using instat graph pad. Difference in the treatment groups was considered significant at (P<0.05) and highly significant at (p<0.01). Subjective parameters were analyzed by Friedman test, Kruskal-Wallis with Dunn's multiple comparison tests and objective parameters were analyzed by ANOVA with Tukey Kramer multiple comparision test and student " t" test.

OBSERVATIONS AND RESULTS

In Table No. 2 Statistical test used is Friedman test with post test for intra-group comparison and Kruskal-Wallis test with Dunn's multiple comparison tests for inter-group comparison. a- p<0.05 with respect to control day 0, b- p<0.05 with respect to control day 15, c- p<0.01 with respect to test day 0, d- p<0.01 with respect to test day 15.In inter group comparison is considered significant (p<0.05) at 30th day of control group vs 0 day test group, (p<0.01) at 45th and 60th day of control group vs 0 and 15th day of test group.(p<0.01) at 60th day of test group vs 0and 15th day of control group respectively. In Table No. 3 Statistical test used is Friedman test with post test for intra-group comparison and Kruskal-Wallis test with Dunn's multiple comparison test for inter-group comparison. a- p<0.05 with respect to control day 0, b- p<0.01 with respect to control day 0, c- p<0.001 with respect to test day 0.

Table 1. Demographic Profile of Patients

Parameter	No. of patients (N)	Percentage (%)
Age in years (Mean=42 years)		
31-40	10	33.33%
41-50	13	43.33%
51-60	7	23.34%
Total	30	100%
Gender		
Male	19	63.33%
Female	11	36.66%
Diet		
Mixed diet	22	73.33%
Vegetarian	4	26.67%
Family History		
Present	19	63.33%
Absent	11	36.66%
Socioeconomic status		
Upper	4	13.33%
Upper middle	3	10%
Lower middle	9	30%
Upper lower	10	33.34%
Lower	4	13.33%
BMI (kg/m^2)		
18.5 to 25 Normal	7	23.33%
Overweight 25 to 30	12	40%
Obese ClassI 30 to 35	8	26.67%
ObeseClassII 35 to 40	3	10%
Physical activity		
Sedentary	12	40%
Mild	13	43.33%
Moderate	5	16.67%
Hard work	0	0%
Smoking		
Smoker	14	46.67%
Non Smoker	16	36.66%

Table 2. Effect of drug on Palpitation in atherosclerosis risk patients (Median scores with Ranges in bracket)

Group	Assessment days				
	0 day	15^{th} day	30^{th} day	45^{th} day	60^{th} day
Control n=10	2{1,3}	2{1,3}	$1\{1,2\}^{c}$	$1\{1,1\}^{a,b,c,d}$	$1\{1,1\}^{a,b,c,d}$
Test n=20	2{1,3}	2{1,3}	2{1,3}	$1\{1,2\}^{c,d}$	$1\{1,1\}^{c,d,a,b}$

Inter group comparison is considered significant (p>0.01) at $30^{th,}$ 45^{th} and 60^{th} days of control group vs 0 day test group, (p>0.01) at $30^{th,}$ 45^{th} and 60^{th} days of test group vs 0 day control group. In Table No. 4 Statistical test used is Friedman test for intra-group comparison and Kruskal-Wallis test with Dunn's multiple comparison tests for inter-group comparison. a- p<0.001 with respect to test day 0, b- p<0.05 with respect to test day 15. Inter group comparison was considered significant (p>0.01) at 30 th, 45th and 60th day with respect to test day 0, and significant (p<0.05) at 45 th, 60th day in test group with respect to control day 0. In Table No. 5 Statistical test used is Friedman test for intra-group comparison and Kruskal-Wallis test with Dunn's multiple comparison tests for inter-group comparison, a- p<0.05 with respect to control day 0, b- p<0.001 with respect to test day 0, c- p<0.05 with respect to test day 15. Inter group comparison is considered significant (p>0.05) at 15th day of control group vs 0 day test group,also (p<0.01) at 30th, 45th and 60th day of control group with respect to test day 0and15 respectively. (p<0.05) at 30th day of test group vs 0 day control group also (p<0.01) at 30th,45th, 60th, day of test group vs control group 0. In Table No. 6 Statistical test used is Paired't' test, for intra-group comparison and one-way ANOVA with post test for inter-group comparison.

Table 3. Effect of drug on Breathlessness in atherosclerosis risk patients (Median scores with Ranges in bracket)

Group	Assessment days				
	0 day	15th day	30th day	45th day	60th day
Control n=10	2{1,3}	1{1,2}	1{1,2} a,c	1{1,1} b,c	1{1,1} b,c
Testn=20	2{1,3}	2{1,2}	1{1,2} c,a	1{1,1} c,a	1{1,1} c,a

Table 4. Effect of drug on Headache in atherosclerosis risk patients (Median scores with Ranges in bracket)

Group	Assessment days				
	0 day	15th day	30th day	45th day	60th day
Control n=10	1{0,2}	0.5{0,1}	0{0,1}a	0{0,1}a	0{0,0}a
Test n=20	1{0,2}	1{0,2}	0{0,1} a	0{0,0} a ,b	0{0,0} a, b

Table 5. Effect of drug on Chest pain in atherosclerosis risk patients (Median scores with Ranges in bracket)

Group	Assessment days				
	0 day	15th day	30th day	45th day	60th day
Control n=10	1{0,1}	0{0,1}b	0{0,0} a,b,c	0{0,0} a,b,c	0{0,0} a,b,c
Test n=20	1{0,2}	1{0,2}	0{0,1} b,a	0{0,1} b,a	0{0,0} b,c,a

Table 6. Effect of drug on Blood Pressure in atherosclerosis risk patients (Mean ± SEM)

BLOOD PRESSURE	TEST GROUP		CONTROL GROUP	
	BT	AT	BT	AT
SYSTOLIC	152.85±1.80	128.5±1.41*	146.9±1.98	123.5±1.83*
DIASTOLIC	91.5±1.62	83.2±0.75*	92±1.10	82±0.81*

Table 7. Effect of drug on Serum Cholesterol in atherosclerosis risk patients (Mean ± SEM)

Group	Assessment days				
	0 day	15th day	30th day	45th day	60th day
Control n=10	215.6 ± 10.441	193.1 ± 10.909	203.4 ± 15.181	208.9± 12.271	212.2 ± 8.712
Test n=20	192.3 ± 6.915	200.65 ± 7.314	193.55 ± 5.944	193.65 ± 5.370	198.9± 5.378

Table 8. Effect of drug on Serum Triglycerides in atherosclerosis risk patients (Mean ± SEM)

Group	Assessment days				
	0 day	15th day	30th day	45th day	60th day
Control n=10	230.1 ± 25.825	233.9 ± 24.014	231.1 ± 28.822	250 ± 25.629	262.4 ± 34.259
Test n=20	261.75±15.929	251.2 ± 19.982	213.15 ±12.849	234.25±27.387	247.25±22.185

Table 9. Effect of drug on LDL-C in atherosclerosis risk patients (Mean ± SEM)

Group	Assessment days				
	0 day	15th day	30th day	45th day	60th day
Control n=10	130.12 ± 8.305	105.8 ± 7.786	115.02±14.117	116.5 ±10.387	105.99 ±10.266
Test n=20	104.485±6.821	110.06 ± 9.302	107.61 ± 7.344	104.835±7.325	100.575 ±7.088

Table 10. Effect of drug on HDL-C in atherosclerosis risk patients (Mean ± SEM)

Group	Assessment days				
	0 day	15th day	30th day	45th day	60th day
Control n=10	39.4 ± 2.684	40.7 ± 2.343	42.1 ± 1.804	42.4 ± 2.353	53.6 ± 3.426 a,b
Test n=20	39.1 ± 1.614	40.35 ± 1.417	40.6 ± 1.171	41.95 ± 1.545	48.85± 2.77 b

Table 11. Effect of drug on MDA (Malondialdehyde) in atherosclerosis risk patients (Mean ± SEM)

Group	Assessment day	
	Before Treatment	After Treatment
Control n=10	38.06 ± 7.25	19.02 ± 2.69*
Test n=20	38.75 ± 5.85	21.48 ± 2.46*

Table 12. Effect of drug on Haematocrit in atherosclerosis risk patients (Mean ± SEM)

Group	Assessment days				
	0 day	15th day	30th day	45th day	60th day
Control n=10	37.65 ± 1.506	36.75 ± 1.692	37.06 ± 1.489	37.02 ± 1.698	36.78 ± 1.667
Test n=20	38.46 ± 0.8016	36.945±0.9512	37.55 ± 0.9517	37.975 ±0.9872	36.54 ± 1.104

Table 13. Comparative Evaluation of Control and Test drug on Safety Parameters, Baseline vs. 60thday (Mean ± SEM)

Parameters		Test (n=20)		Control (n=10)	
		B.T.	A.T.	B.T.	A.T.
Hb%		12.765 ± 0.2589	12.315±0.3576	12.55 ±0.5021	12.26±0.5558
TLC		7760 ± 399.83	8145 ± 354.87	7525 ± 619.11	7645 ± 566.88
DLC	P	56.3 ± 1.673	61.1 ± 1.117	59.9 ± 2.479	59.1 ± 2.562
	L	37.45 ± 1.688	33.45 ± 1.120	34.5 ± 2.409	35.3 ± 2.716
	E	3.55 ± 0.2348	3.5 ± 0.2351	3.3 ± 0.2134	3.9 ± 0.2769
	M	2.65 ± 0.2436	1.95 ± 0.2112	2.3 ± 0.2134	1.7 ± 0.2134
	B	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00
Blood Urea		29.05 ± 1.204	29.75 ± 1.953	32 ± 2.404	31.3 ± 4.137
Serum Creatinine		0.98 ± 0.07348	0.935 ± 0.05585	1.04 ± 0.1752	1.01 ± 0.07667
SGOT		23.9 ± 1.957	22.8 ± 2.022	29.8 ± 4.988	27.5 ± 6.970
SGPT		28.85 ± 2.956	26.05 ± 3.722	34.8 ± 8.403	29.3 ± 6.389

In Table No. 13, Test used, paired't' test, $p > 0.05$.

In test group on 60th day was statistically significant with respect to 0 day test and 0 day control $p<0.05$, but not statistically significant with respect to 60th day control. Control group also showed significant reduction in serum concentration of MDA on 60th day with respect to 0 day test and 0 day control. In Table No. 7, Statistical test used is (ANOVA) one way with tucky kramer multiple comparision test. p value >0.05. In Table No. 8, Statistical test used is (ANOVA) one way with tucky kramer multiple comparision test. p value > 0.05. In Table No. 9, Statistical test used is (ANOVA) one way with tucky kramer multiple comparision test. p value > 0.05. In Table No. 10, Statistical test used is (ANOVA) one way with tucky kramer multiple comparision test. a- $p<0.01$with respect to control day 0,15.30,45. b- $p<0.01$ with respect to test day 0,15,30,45. Inter group comparison, $p<0.01$. Inter group comparison was significant ($p<0.01$) at 60th day of control group VS test group 0,15th day respectively. also significant ($p<0.01$)at 60th day of control group VS test group 30th,45th day respectively. In Table No. 11, Statistical test used is Paired't' test, for intra-group comparison and one-way ANOVA with post test for inter-group comparison. P value is 0.0187 in control group considered significant, p value is 0.0038 in test group considered very significant and Inter group comparison was significant ($p <0.05$) in test group on 60th day with respect to baseline. In Table No. 12, Statistical test used is (ANOVA) one way with tucky kramer multiple comparision test. P value > 0.05.

DISCUSSION

In our study 63.33% (19) subjects had positive family history of cardiovascular diseases and the remaining 36.6% (11) subjects had no family history of CVD. (Table.8) Arvind K *et. al.* found that the Family history of CAD is associated with markers of subclinical atherosclerosis, and this relationship remains statistically significant after adjusting for traditional risk factors.

Our results are in accordance with Arvind K *et. al.* (2013). In our study 40% (12) subjects were overweight, 26.66% (8) were belonged to obese class I, 23.33% (7) were normal, 10% (3) were belonged to obese class II. (Table.1) Our study population comprised of 76.67% subjects with body weight above normal. Irace C**,** found that increasing body weight favours the clustering of coronary heart disease risk factors (Irace *et al*., 2009). In present study 40% (12) subjects were found with sedentary life style, 43.33% (13) with mild physical activity, and 16.67% (5) with moderate physical activity. In this study 83.33% subjects constitute low levels of physical activity which increases the risk of atherosclerosis because regular physical activity (eg, 30 to 45 min of walking, running, swimming, or cycling 3 to 5 times/wk) reduces incidence of some risk factors (hypertension, dyslipidemia, diabetes), CAD (eg, MI), and death attributable to atherosclerosis in patients with and without previous ischemic events. Whether the association is causal or merely indicates that healthier people are more likely to exercise regularly is unclear. Optimal intensity, duration, frequency, and type of exercise have not been established, but most evidence suggests an inverse linear relationship between aerobic physical activity and risk (http://www.merckmanual.com/professional/ cardiovascular disorders/arteriosclerosis/atherosclerosis.html).

In present study 36.67% (11) subjects were females all were non smokers, whereas 63.33% (19) subjects were males out of which 46.66% (14) were smokers and 16.67% (5) were non smokers. Cigarette smoke increases the incidence of atherosclerosis and its resulting mortality is due to the toxic effects of smoke on the mechanisms of atherosclerosis, thrombosis, vasomotor system and arrhythmia, smoking increase the risk factors of atherosclerosis and cardiovascular morbidity (Ansari *et al*., 2012). In present study test group showed significant reduction in palpitation, after treatment as compared to before treatment. Control group showed significant reduction in these symptoms score on 60th day with respect to baseline .The result indicated that both group were

equally effective in reducing palpitation, breathlessness, headache and chest pain. The test group showed significant reduction in Systolic and diastolic BP after treatment as compared to before treatment. The result indicated that both groups were equally effective in reducing Blood Pressure. The endothelium regulates blood flow and pressure and is easily damaged by oxidative stress which increases the risk of atherosclerosis. In oxidative stress NO a vasodialator agent derived from endothelium decreases, resulting in vasoconstriction (Soydinc *et al*., 2007), high blood pressure, breathlessness, palpitation, chest pain and headache. As Badranjboya significantly decreases MDA concentration which is a marker of lipid peroxidation (oxidative stress), it indicates antioxidant effect of Badranjboya. Thus it increases the release of NO from endothelium and improves the vascular elasticity which results in decrease in blood pressure, palpitation, breathlessness, headache and chest pain. When the Mean ± SEM score of total serum cholesterol, serum Triglycerides and LDL-C of both groups were compared, the difference was statistically not significant in both intergroup and intragroup comparisons ($p>0.05$). When the Mean ± SEM serum HDL cholesterol of both groups were compared statistically, the difference was significant on both intergroup and intragroup comparison ($p<0.01$). It was found that the difference between Mean ± SEM concentration of MDA in test group on 60^{th} day was statistically significant with respect to baseline ($p<0.05$).

Control group also showed significant reduction in serum concentration of MDA on 60^{th} day with respect to 0 day. MDA is a marker of oxidative stress and in many studies it showed highly significant relation with coronary artery disease revealing the interrelation between the oxidative stress and atherosclerosis. The role of the oxidative stress and CAD is well known. The MDA a carbonile group produced during lipid peroxidation is used widely in determining oxidative stress. Increased MDA levels in CAD were demonstrated in several studies (Soydinc *et al*., 2007). Decrease in MDA concentration indicates decrease in lipid peroxidation, it means release of NO from endothelium increases which is a vasodilator thus decreases the tension in vessels. NO also inhibit thrombocyte aggregation, leucocyte adhesion, smooth cell proliferation, and LDL oxidation (Soydinc *et al*., 2007).

Above findings showed that the total serum cholesterol, LDLc and Triglycerides remains unchanged in both groups, while HDLc increased significantly and MDA concentration reduced significantly. Therefore the present study reveals that the Badranjboya (*Nepeta hindostana*) possess antioxidant activity and anti atherosclerosis activity. During the 1980s, some researchers began to recognize that LDL itself was not a reliable independent risk factor for CHD; half of those who suffer CHD have LDL levels within normal limits. Among the 28,000-plus participants of the Womens Health Study, for example, 46% of first cardiovascular events occurred in women with LDL cholesterol levels less than 130 mg/dL, the desirable target for primary prevention set by the National Cholesterol Education Program (NCEP). Research in both animals and humans has shown that oxidized LDL is a better predictor of atherosclerosis and cardiovascular disease than regular LDL cholesterol. Whether or not oxidized LDL is a direct contributor to the atherogenic process cannot be determined with any certainty based upon the available evidence. The stronger association between oxidized LDL and cardiovascular disease suggests that a person's antioxidant status is a far more important determinant than LDL levels of the risk of developing advanced plaques. In animal studies, administration of antioxidant drugs like probucol impairs LDL oxidation and arterial plaque formation, even when there is no change in blood cholesterol levels. In fact, administration of the antioxidant butylated hydroxytoluene (BHT) significantly reduces the degree of atherosclerosis in the aorta of rabbits, even though it raises LDL cholesterol levels. A similar phenomenon is observed in humans. Among elderly Belgians, higher levels of oxidized LDL were accompanied by a significantly increased risk of heart attack, regardless of total LDL levels. However, there was no association between oxidized LDL concentrations and total LDL levels (Anthony, 2005).

Decrease in MDA concentration after the use of badranjboya indicates its antioxidant effect. Thus it might have reduced oxidation of LDL and also the risk of atherosclerosis. Our study showed significant increase in HDL cholesterol. High-density lipoproteins (HDLs) oppose atherosclerosis directly, by removing cholesterol from foam cells, by inhibiting the oxidation of LDLs, and limiting the inflammatory processes that underlie atherosclerosis. HDLs also have antithrombotic properties. Thus, HDL-cholesterol interrupts the process of atherogenesis at several key stages. HDL-cholesterol prevents atherogenesis by inhibition of monocyte adhesion, inhibition of LDL-cholesterol oxidation and MCP-1 expression and antithrombotic properties of HDL-cholesterol (Philip Barter, 2005). High density lipoproteins (HDL) have been reported to inhibit oxidation of low density lipoproteins (LDL) based in part on observations that oxidative changes occur more slowly in LDL-HDL mixtures than in LDL alone. Tribble DL in a study observed that HDL directly inhibits per oxidative stress within the LDL particle in the presence of both Cu2+ and Fe3+. (Tribble *et al*., 1995) The prevention of lipoperoxide generation during copper-induced LDL oxidation by HDL could be due to their enzyme content, such as paraoxonase (Morena *et al*.). Triglycerides as far as is currently known, are not directly atherogenic but represent an important biomarker of CVD risk because of their association with atherogenic remnant particles and apo C-III, a pro inflammatory, pro atherogenic protein found on all classes of the plasma lipoproteins**.** Hypertriglyceridemic states are associated with increased VLDL production and delayed VLDL clearance from circulation (Beatriz, 2011). The difference was statistically not significant in both intergroup and intra group comparison of Mean ± SEM score of Haematocrit value $p>0.05$. However the decrease in haematocrit value is only 2% but there was consistent decrease in the blood viscosity.

Therefore the present study reveals that *Badranjboya* has preventive effect for atherosclerosis. Previous supporting studies revealed that *Badranjboya* possess antioxidant activity (Mimica-Dukic, 2004) According to Unani medicine atherosclerosis is a type of *Amraze Majari* in which *Sharain* (arteries) become narrow or obstructed. It is induced by *Dusumate Dam* caused by *Akhlaate Ghaleeza* (Vicid Homours), *Akhlate Lazija*, (Sticky Homours) and sometimes by *Akhlaate Kaseera* (Excess Humours). The obstruction of the vessels results in closure of the pathways for release of *"Riyah"* which is responsible for pain and closes the pathway for *"Rooh"* that may lead to sudden death (Jurjani, 1903). *Ibne Sina* has described two important measures for the prevention and treatment of *Dusumate dam,* its related conditions and obstructions; first by decreasing the viscosity of *Akhlat*

(making humours less viscous) and second by *Ishaal* (diarrhoea/ purgation) and *Idrar* (diuresis) (Ibn Sina, 2007). By these two measures the excessive *Akhlat* (humour) are removed from the vessels, the *Tamaddud* (pressure) in vessels also decreases and the vascular flexibility is maintained. The abnormal humours accumulated in vessels that are mainly responsible for narrowing the arteries (especially coronary artries) can be washed away. In Unani classical literature the test drug Badranjboya is reported to be *Mufarrah wa Muqawwi Qalb* (cardiotonic)*, Mulattif*, *Mufatteh sudud*, *Muhallil* and *Mus'hil* and it is recommended for the prevention and treatment of *Khafqaan* (Palpitation) *Usre Tanaffus* (breathlessness), *Falij* (Paralysis), *Laqwa* (Facial palsy), *Amraze balghami wa saudavi*. Badranjboya by virtue of its *Muhallil* property resolves the morbid matter and liquefies the humours, and by *Mulattif* effect breaks the *Akhlate Lazija* in small pieces which are evacuated from the vessels easily. By its *Mufatteh* (vasodialator) effect reduces the vascular pressure, widens the lumen and thus facilitates smooth flow of humours. *Mus'hil* property is responsible for the removal of wastes. Thus the mechanism proposed by the Unani physicians, appears to be comprehensive and commensurates the modern approach of treatment.

In control group serum cholesterol, Triglycerides LDL-c remains unchanged, HDL-C increases significantly after treatment, MDA and Blood pressure reduces significantly after treatment, Haematocrit % reduced only by 1%.Garlic is an important drug in the alternative system o medicine. It has been thoroughly researched. Experimental and clinical studies confirm that the ancient experience with beneficial effect of garlic hold validity even in prevention of cardiovascular disorders and other metabolic ills. Recent data published after year 2000 convincingly point out the garlic and its various forms reduce cardiovascular risk, including abnormal plasma lipids, oxidised low density lipoprotein (LDL) abnormal platelet aggregation and a high blood pressure. Stimulation of nitric oxide generation in endothelial cells seems to be the critical preventive mechanism. Garlic may promote an anti inflammatory environment by cytokine modulation in human blood. Cardio protective effect of dietary garlic is mediated in large part via the generation of hydrogen sulphide (H_2S). Garlic derived organic polysulphides are converted by erythrocytes in to hydrogen sulphide which relaxes vascular smooth muscle, induces vasodilatation of blood vessels, and significantly reduces blood pressure. There are data on potential ability of garlic to inhibit the rate of progression of coronary circulation (Ginter, 2010). Badranjboya appears to hold promise in reducing the risk of CVD. Present study indicates potential ability of badranjboya to inhibit the rate of progression of atherosclerosis. More research should be carried out on large scale to critically evaluate the benefits of this important herb.

Conclusion

From the present study, it can be concluded that: *Garlic*, known drug with anti oxidant activity, has got the similar effect as that of the test drug *Badranjbooya.* Badranjbooya effectively showed reduction in LDL oxidation. Badranjbooya showed anti atherogenic effect in the present study as it increases HDL-C and reduces MDA concentration significantly. The antioxidant effect was prominent despite showing no change in production of total cholesterol, LDL and Triglycerides. These effects illustrate the latest trend of effective management of CVD risk by the use of *Badranjboya*. Present study indicates potential ability of *Badranjboya* to inhibit the rate of progression of atherosclerosis. It can be concluded that *Badranjboya* should be administered with other treatment modalities like weight normalization for obese patients, physical therapy, dietary modification etc. for optimal results.

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