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A randomized single blinded preliminary clinical study on lipid lowering effect of a polyherbal compound in the management of hypercholesterolemia

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Abstract
Hypercholesterolemia is a common lipid metabolic disorder characterized by an abnormal concentration of lipids or lipoproteins in blood. Uncontrolled or improper treatment leads to complicated serious illnesses such as cardio vascular, cerebro vascular and peripheral vascular diseases. According to the World Health Organization a third of ischaemic heart disease is attributable to high cholesterol. Globally hypercholesterolemia is estimated to cause 56% of ischaemic heart diseases and about 4.4 million deaths per year. The objective of the study was to evaluate the efficacy and safety of Polyherbal compound in the management of hypercholesterolemia. A Randomized single blinded preliminary clinical study was conducted from February 2014 to August 2014 in the outpatient department of National Ayurveda Teaching Hospital, Borella. 30 patients of hypercholesterol, aged 40-60 years from both gender were selected. The patients were received 30ml of Polyherbal compound juice two times a day for 21 days with dietary restriction and moderate physical exercise for 45 minutes. The pre and post study effects were assessed by symptom reduction and laboratory reports. The results showed statistically significant reduction in total cholesterol (TC), serum triglycerides (TG), Low Density Lipoprotein (LDL), TC/LDL ratio and LDL/HDL ratio and increase of High Density Lipoprotein (HDL). Our results demonstrated that the Polyherbal compound has beneficial effects on reduce lipid profile without any adverse effects. Therefore, further high quality studies with large sample should be conducted to better understanding the effectiveness of Polyherbal compound on hypercholesterolemia.

Keywords: hypercholesterolemia; metabolic disorder; polyherbal compound

1. Introduction
Hypercholesterolemia is a metabolic disorders of lipid and lipoproteins, in other words increased concentration of total cholesterol, triglycerides, LDL cholesterol and decreased concentration of HDL cholesterol [1]. Hyperlipidemia is a major contributor to the pathogenesis of cardiovascular diseases like coronary artery diseases, ischemic cerebro vascular and peripheral vascular diseases [2]. Framingham study showed that a 1% increase in total cholesterol cause 2% increase in the incidence of IHD [3]. Atherosclerosis is now considered as an inflammatory disease as it is a result of inflammation and inflammatory cytokines, are prevalent in atherosclerotic plaques [3]. Cardiovascular disease (CVD), such as coronary heart disease, stroke, peripheral artery disease, is the leading cause of mortality worldwide. Estimates from the World Health Organization suggest that in 2008, approximately 17.3 million individuals died from CVD, corresponding to 30% of global deaths. By 2030, almost 25 million individuals are expected to die from CVD, primarily heart disease and stroke. Risk factors for CVD are well documented and include lifestyle choices such as smoking and a sedentary lifestyle, and metabolic disorders such as obesity, diabetes and hypercholesterolemia [4]. Hypercholesterolaemia is among the most common health problems treated with traditional remedies [5].
Over the last two decades there has been an increasing emphasis placed on screening for high cholesterol and adopting intervention to reduce cholesterol levels in order to reduce risks. Globally hypercholesterolemia is estimated to cause 56% of ischaemic heart diseases and about 4.4 million deaths per year [6]. Despite the use of numerous newer lipid lowering drugs, due to its high cost and adverse effects, the society are now diverting to certain natural substances.
Hypercholesterolemia represents one of the major risk factors for atherosclerosis affecting arteries of large and medium size and consequently causing ischemia in the brain, heart, or legs. Coronary artery disease and cerebral stroke represent the major causes of morbidity and mortality among elderly and middle aged subjects [7].
Lipids are a group of heterogeneous metabolically active substances constantly moving in the circulation and existing in estate of dynamic equilibrium between peripheral tissue, gastrointestinal tract, and liver [8]. Almost all the lipoproteins are formed in the liver, which has active enzyme system for synthesizing triacylglycerol, phospholipids, cholesterol, plasma lipoproteins and for converting fatty acid to ketone bodies. In the process of metabolism LPL (Lipoprotein lipase) enzyme, secreted from liver cells is responsible for catabolic activity upon lipid and lipoprotein to maintain the equilibrium of lipid concentration. Hypercholesterolemia is being increasingly recognized as an important contributory factor towards the development of CVD.
In Unani system of medicine, there is concept of *Quwte Tabaiyah* (natural power), which serves the functions of

nutrition, growth and reproduction in the body, and expel out waste products (*Fuzlat*) from the body. Liver is the chief organ of *Quwate Tabaiyah*. *Quwate ghazia* (nutritive power) is one of the types of *Quwate Tabaiyah* which is responsible for ingestion, digestion, absorption, transformation and assimilation of *ghiza* (food) and excretion of waste products. *Quwate Ghazia* is served by four kinds of subordinative faculties. *Hazme Kabidi (liver digestion)* is one of the parts of *Quwate Hazma* i.e. type of subordinative facuty of *Quwate Ghazia*. *Hazme Kabidi* is aimed at benefitting the liver cells themselves as well as the entire body [9].

Hypercholesterolemia, as such has not been described in Unani literature but it may be interpreted with the abnormalities of entire mechanism of *Hazme Kabidi*.

There are three conditions which affects *Hazme Kabidi* i.e. *Baroodate jigar* (coldness of liver), causes hindrance in digestion of food, which is reached to liver from intestine. Second is obstruction by viscous matter or any inflammation which causes partial digestion of nutrients. Third is the nutrition resulting from alteration in quantity or quality (*Kammiyat* and *Kaifiyat*) of food [10].

Unani system of medicine have recommended a number of drugs, which are *Haar* (hot) in *Mijaz* (temperament) to modulate liver functions. Keeping these facts in mind, this study was conducted to evaluate the efficacy and safety of Polyherbal compound in hypercholesterolemia. The poly herbal formula consists of curry leaves (*Murraya koenigii)* [11], black seeds (*Nigella sativa*) [12] and fenugreek seeds (*Trigonella foenum graecum*) [13], which had been used by the Unani physicians to reduce blood cholesterol level in human being and also scientifically reported to have lipid lowering effects of these herbs.

Dietary restriction, moderate physical exercise and drug therapy have shown promising results to regulate HDL and LDL cholesterol levels and to reduce subsequent risk of coronary artery disease associated pathological conditions. But due to high cost and adverse effects of lipid lowering drugs, peoples are now diverting to certain natural substances.

The aim of the study was to evaluate the efficacy and safety of Polyherbal compound in the management of hypercholesterolemia.

2. Methodology

The trial was conducted from February 2014 to August 2014 in the outpatient department of National Ayurveda Teaching Hospital, Borella. 30 diagnosed patients of hypercholesterol from both genders between 40-60 years of age and who willing to follow the informed consent and comply with the study procedures were selected. The patients were received 30ml juice of Polyherbal compound on empty stomach for 21 days with dietary restriction and moderate physical exercise for 45 minutes (strictly adhere with 45 minutes' walk early morning or late evening on empty stomach at least 5 days per week on regular basis). Inclusion criteria: Diagnosed patients of hypercholesterolemia, patients of both sexes, age group 40-60 years of age and patients able to follow the instructions. Exclusion criteria: Subjects below the age of 40 and above the age of 60, pregnancy and lactating mothers, sever cardiovascular, renal, liver diseases, AIDS and T.B., diabetes mellitus, hypothyroidism and patients who fail to fallow up. Concomitant treatment was not allowed during the treatment, the patients who were taking any other medicines as a treatment of hypercholesterolemia were advised to abstinence for a week from consuming those drugs before commencing the treatment. Subjective parameters: Palpitation, Breathlessness, and Joints pain. Objective parameters were total cholesterol (TC), serum triglycerides (TG), Low Density Lipoprotein (LDL), TC/LDL ratio and LDL/HDL ratio and increase of High Density Lipoprotein (HDL) ratio.

Study Design

A Randomized single blinded preliminary clinical study.

Statistical Analysis

The data were collected and tabulated, which were statistically analyzed by calculating the mean and standard deviation followed by repeated measure of ANOVA with paired-t tests to the observational records at interval of zero day, 7th day, 14th day and 21st day.

3. Results and discussion

Thirty patients of diagnosed hypercholesterolemia between 40-60 years age, with history of palpitation, breathlessness and joints pain were treated with a juice of polyherbal formula. The demographic characteristics of the study population are shown in Table- 01.

Table 1: Demographic Data

S. No.	Demographic data		No of patients
01	Age (mean ± SEM)		45.3± 1.16
02	Sex	Male	13
		Female	17
03	Dietary habits	Veg.	03
		Non veg	27

The pre and post study effects were assessed by symptoms reduction and laboratory reports. The results showed statistically significant reduction ($p< 0.05$) in serum cholesterol, triglycerides (TG), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL) and serum cholesterol/HDL ratio. Subjective parameters were measured on day 0, 7, 14 and 21 (Table-02). At the end of 21st day it was found that palpitation, breathlessness and joints pain associated with hypercholesterolemia were significantly reduced ($p<0.01$).

Table 2: Effect of the polyherbal compound on the subjective parameters in hypercholesterolemia

Symptoms	Assessment days (Mean ± SEM and Median rating with range in brackets) (n= 30)				
	0th day	7th day	14th day	21st day	P value
Palpitation	1.67 ± 0.27 2(0,3)	1.60±0.25 2(0,3)	1.33±0.25 2(0,3)	0.60±0.16* 1(0,2)	0.01
Breathlessness	2.27±0.12 2(2,3)	2.27±0.12 2(2,3)	1.70±0.18 2(1,3)	0.87±0.19* 1(0,2)	0.01
Joints pain	2.33±0.25 3(0,3)	2.33±0.25 3(0,3)	2.00±0.24 2(0,3)	1.33±0.18* 1(0,2)	0.01

The results of objective parameters showed statistically significant reduction in serum cholesterol, triglycerides, LDL, and serum cholesterol/HDL ratio, with significant increase of HDL (Table-03).

Table 3: Effect of the polyherbal compound on the objective parameters in Hypercholesterolemia.

Objective parameters	Mean ±SEM and Median rating with range in bracket		
	Before treatment	After treatment	P value
Serum cholesterol	231.73± 5.29	208±3.76*	0.05
	235(200, 265)	206(185,235)	
Triglycerides	210.93± 11.00	191.06± 9.92*	0.05
	186(160, 278)	165 (145, 245)	
HDL cholesterol	43.93±1.85	50.20±1.58*	0.05
	43(35, 60)	48(44, 63)	
LDL cholesterol	127.07±9.48	116.73±8.07	ns
	120(72, 175)	112(70, 160)	
Cholesterol/HDL	5.39± 0.24	4.21± 0.14*	0.05
	5.58(3.81, 6.67)	4.38(3.17, 5.22)	

Before starting the treatment 100% patients had breathlessness, 93% had joints pain and 80% had palpitation. After the treatment 66.7% patients had breathlessness, 87% of joints pain and only 53% with palpitation respectively (Table - 04).

Table 4: Overall effect of the polyherbal compound in hypercholesterolemia

Parameters	0th day	14th day	21st day	P value
Breathlessness	30	25	12	p>0.05
Joints pain	28	20	09[b]	P<0.01
Palpitation	24	18	12[c]	P<0.05

Our study demonstrated a decrease in TC, TG, and LDL levels and an increase in HDL with daily ingestion of 30 ml polyherbal juice. Even, the decrease in LDL and TG are sufficiently enough predictor for the beneficial effect of polyherbal juice. Medicinal plants play a key role in preventing various diseases. [2]

The effects of *Nigella sativa* consist of flavonoids and carvone have strong anti-oxidant activity which might be involved in hypolipidemia. A study shown that the aqueous extract of *Nigella sativa* decrease lipid levels in diet induced hyperlipidemic rats [2].

N. sativa oil and seeds have been widely used to management of different diseases within centuries and regarded as important drug in traditional medical system (Ayurveda, Unani, Arabic and Chinese medicines) in Asian and Middle East countries and also recommended for regular use in Tibb-e-Nabwi [14]. *Nigella sativa* is commonly used medicinal plant which has been used for thousands of years in traditional system of medicine for example, Ayurveda, Unani, Arabic and Chinese medicine. It is claim that Prophet Muhammad (PBUH) said "Use Black seed regularly, since it is a cure for every disease except death [15]. The seeds of fenugreek (Trigonella foenum graecum L.) are traditionally assumed to have restorative properties. A recent study shown that the fenugreek seed extract containing steroid saponins increased food consumption and induced hypocholesterolemia in rats. Both in normal and diabetic rats, steroid saponins decreased total plasma cholesterol without any change in triglycerides [16]. on contrary to this study in 2000, another study was conducted to investigate the hypolipidemic effect of fenugreek in hypercholesterolaemic patients and he found that the fenugreek powder has the property to reduce serum cholesterol, triglycerides and VLDL levels significantly [17]. This finding is supported with another study that the ethanol extract from *Trigonella foenum* seeds contained hypocholesterolemic components which appear to be saponins that interact with bile salts in the digestive tract [18].

Amongst the green leafy vegetable the total antioxidant activity was the highest in *Murraya koenigii* (2691 micromol of ascorbic acid/gm sample) as compared to that of methanol extracts of Amaranthus sp., *Centella asiatica* and *Trigonella foenum graecum*. [11] Antioxidant property of curry leaves helps to protect from high cholesterol level, cardiovascular diseases, diabetes and many other degenerative illnesses [19]. *Murraya koenigii* leaves contains alkaloid carbazole has the property to reduce cholesterol level in the blood. A study revealed that the ethanolic extract of curry leaves possessed potent antioxidant properties which may be due to the presence of biological active ingredient carbazole alkaloids, glycoside, triterpenoids and phenolic compounds [20].

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