

Evaluation of the Effect and Efficacy of Cold Water Extract of New Herbal Formulation on Serum Lipid Levels in the Management of Hyperlipidaemia

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Abstract

This randomized prospective cohort clinical study was done to evaluate the effect of cold water extract of new herbal formulation consisting of Allium sativum (Bulb) Piper nigrum (Nuts) Murrayakoenigii (Leaves) in managing hyperlipidaemic conditions of patients in comparison to the effect of dietary management. After 14 days treatment, patients of the group A, which received cold water extract showed 19.3% decrease in serum total cholesterol level in comparison to the level of same parameter before the treatment ($p < 0.05$) whereas it showed statistically significant decrease in serum triglyceride (29%), LDL (26.5%) and TC:HDL ratio (32.3%) but the patients of group B, which received dietary management did not show significant reduction in the serum levels of total cholesterol, triglyceride, LDL and TC:HDL ratio compared to those of before treatment of same group. The patients of group A showed significant decrease in serum concentrations of total cholesterol (16.5%), triglyceride (29.3%), LDL (5.3%) and TC/HDL ratio (21.4%) while showing considerable increase in HDL level in comparison to the serum concentrations of same lipid parameters of Group B after 14 days treatment. Considering the overall results of present study and comparing with the results of previous studies, it is evident that the short term administration of cold water extract of new herbal formulation has shown significant effect in decreasing the elevated serum lipid levels (except to the HDL levels) than the effect of given dietary management alone in hyperlipidaemic patients without causing clinically evident adverse effects.

Keywords: Allium sativum, Piper nigrum, Murrayakoenigii, Hyperlipidaemia

II. Introduction

Heart diseases are one of leading causes of death in the world. High blood cholesterol or hyperlipidaemia is a major risk factor for heart disease. South Asians in the United States have a higher Coronary Heart Disease (CHD) risk, which may be related in part to a higher prevalence of the metabolic syndrome, insulin resistance, and hyperlipidaemia. Hyperlipidaemia has long been associated with the development of cardiovascular diseases (CVD) in industrialized nations [1]. There has been an increase in the prevalence of hyperlipidaemia in developing countries that can partly be attributed to urbanization [2]. There is considerable evidence to suggest that the identification

and treatment of Hyperlipidaemia will reduce the risk of premature CHD before the age of 65 [3]. Management of hyperlipidaemia includes Dietary management, regular exercise, mental relaxation and pharmacological treatments. Pharmacological therapy includes the different classes of synthetic and semisynthetic drugs. HMG-CoA reductase inhibitors, Bile acid sequestrants, Activate lipoprotein lipase, Inhibit lipolysis and triglyceride and others (Ezetimibe and Gugulipid) are the major categories of lipid lowering medicines [4].

From ancient time, herbal medicines have gained significant importance as a main source of effective and safe medicines in primary healthcare worldwide. According to the WHO, 80 % of world population is still dependent on traditional medicines. Cost effective simple herbal preparations would be beneficial in long term management of hyperlipidaemia to reduce the risk of CHD. For this purpose, a simple herbal preparation was formulated by Dr. W. A. L. Chandrasiri Waliwita (D.S.A.M.S (Hons), M.D (Ayur), Senior Lecturer in Kayacikitsa, Gampaha Wickramarachchi Ayurveda Institute, University of Kelaniya, Yakkala, Sri Lanka on the basis of traditional evidences, clinical experiences and scientific evidences to reduce elevated serum lipid levels of patients and to reduce the risk of coronary heart diseases. All plant materials of the new formulation can easily be found in daily home needs. Therefore, patient finds no extra burden in collecting the materials. These materials are commonly used by almost all individual in preparation of food as a spice or flavouring agent. All materials of this formulation consist of many volatile constituents, which are easily evaporated during the process of food preparations. According to the scientific evidence, Garlic has thermolabile compounds, which are easily inactivated during the food processing. Therefore, a strategy was applied to secure the destruction of thermo labile substances and to preserve the volatile constituents so as to enhance the effect and efficacy of the preparation by obtaining a cold water extract of the formulation. According to the previous clinical experiences and evidences observed in case studies, this formulation has shown satisfactory effect in reducing serum lipid levels and symptoms of the uncomplicated coronary heart diseases. On the other hand, cold water extract of this new herbal formulation can be obtained with the use of home utensils

as a homemade remedy. The cost of a single dose of cold water extract is negligible when compared with a dose of conventional hypolipidaemic drugs. Patients experience no difficulty in taking medicine while having their ordinary meals. There is no possibility to produce serious adverse reaction since they are the materials of common use in food preparation. Once prepared the medicine according to the given method of formulation can be stored for several days in a refrigerator without deterioration. Patient can use it purely and freshly as prescribed by the physician. Therefore, it is needed to validate the effect of this formulation through different clinical trials. The primary objective of present study was to determine the effect and efficacy of new herbal formulation in the management of hyperlipidaemic conditions of patients. Specific Objectives included the evaluation of the effect of new herbal formulation on fasting serum lipid levels i.e. Total cholesterol (TC) level, Triglycerides (TG) level, LDL, and HDL in hyperlipidaemic patients, evaluation of efficacy of new herbal formulation on the clinical improvements and to determine the adverse effects on oral administration of new herbal formulation.

1. Materials and Methods

2.1 Plant materials

The herbal formulation consists of three plants materials given in the Table 1 and they were collected by patients as a daily home need.

Table 1: Plant materials used in the new formulation

Scientific Name	Family Name	Sinhala Name	Sanskrit Name	Parts Used
<i>Allium sativum</i>	Alliaceae	<i>Sudalunu</i>	<i>Lañuna</i>	<i>Bulb</i>
<i>Piper nigrum</i>	Piperaceae	<i>Gammiris</i>	<i>Marica</i>	<i>Nuts</i>
<i>Murrayakoenigii</i>	Rutaceae	<i>Karapiica</i>	<i>Kālañāka</i>	<i>Leaves</i>

2.2 Research design

This study was a randomized prospective cohort clinical study. All patients were selected from Hyperlipidaemia clinic of Gampaha Wickramarachchi Ayurveda Hospital. All selected cases had been treated with allopathic medicine previously by qualified practitioners and consultants at their medical clinics. Patients voluntarily visited the Hyperlipidaemia clinic at Gampaha Wickramarachchi Ayurveda Hospital with the intention of having medical advice for unsuccessful controlling of Hyperlipidaemia. Adverse effects of treatment were the prime cause of seeking alternative method of controlling Hyperlipidaemia. Both male and female patients, aged between 20-60 years having evidence of elevated serum lipid profile and body mass index (BMI) of <40 without serious medical conditions were selected for this study. Patient showed the poor lipid control on allopathic medication and withdrawn from medication for more than

three months were selected for this study. Pregnant females, lactating mothers and patients those who have evidence of any major illness like diabetes mellitus, renal insufficiency, cerebrovascular accidents, ischaemic heart diseases and endocrine disorders were excluded. Patients were diagnosed on the basis of criteria recommended by NCEP, (2001) in the diagnosis of hyperlipidaemia.

The selected patients were randomly assigned into two groups (Group A and Group B) consisting of 20 patients for each. The patients of group A were treated with New Herbal Formulation and prescribed dietary management and the patients of group B were instructed to follow the prescribed dietary management (Group B) during the period of 14 days. Assessment was done on the basis of clinical observations including the estimation of blood pressure, pulse rate and body weight and biochemical investigations, which included lipid profile.

2.3 Method of preparation, Dosage and Administration of Herbal Formulation

2.3.1 Method of preparation of new herbal formulation

Allium sativum (Garlic) - 5g (un-damaged 2 lobes)

Piper nigrum (Pippper)- 5g(15 nuts)

Murraya koenigii (curry leaf) - 10g (10 leaves)

Cold water - 125 ml

All patients of group A were instructed and convinced properly to identify and collect the correct herbal materials and to measure required amount of materials. Patients were instructed to peel out the skin of garlic lobes without causing damages to the lobes. Then they were instructed to pour the required volume of cold water into a electric blender cup and to add the peeled garlic lobes, curry leaves and black pepper as prescribed in the formula. Then they were instructed to blend the materials until to obtain a blended mixture of herbal formulation and to keep it in the refrigerator at a temperature below 4⁰C until for use.

2.3.2 Dosage and administration

Patients of group A were instructed to take 2 table spoonful of previously prepared mixture of new herbal formulation diluted with 100ml of cold water with three main meals (Breakfast, Lunch and Dinner) of a day for consecutive 14 days. In addition to this preparation patients were instructed to follow the prescribed method of dietary management, which includes low fat, high vegetable fiber diet. The patients of group B were instructed to follow the method of dietary management only.

2.3.3 Dietary management

Patients were instructed to choose unsaturated fats (olive oil or canola oil instead of coconut oil), whole grains (whole wheat bread or brown rice), fruits and vegetables, which are high in fiber and to limit cholesterol rich diet

including egg yolks, whole milk products and organ meats (Anderson and Davidson, 2000)

2.3.4 Monitoring of patients

All patients were instructed to report any clinical changes, adverse effects and alterations in proper use of prescribed preparation of new herbal formulation and dietary management during the period of study and after 14 days patients were advised to get a serum lipid profile analysis from the recommended clinical laboratory.

2.4 Data processing and analysis

Analysis of variance followed by student's T-Test was done using the Minitab statistical software package. The results were considered as significantly different when the $p < 0.05$. The values of lipid parameters were expressed as the mean \pm standard error of mean (SEM).

3. Results and Discussion

40 patients of having confirmed hyperlipidaemic conditions were selected for the present study and all patients were between 31 – 60 years of age. The majority of patients were between 51-60 years of age (Table 9, Figure 1). 57.5% of patients selected for the study were male. The female to: male ratio was 1:1.35.

Table 2– Age distribution of selected patients

No	Age	Total	Percentage
1	21-30	00	00%
2	31-40	08	20%
3	41-50	12	32%
4	51-60	20	48%

3.1 Effects on serum lipid concentrations

At the first visit to the clinic, almost all patients of the sample had shown poor cholesterol control even though they had been treated with allopathic medicine previously. Before the commencement of study all patients showed highly elevated serum levels of total cholesterol and LDL. The concentration of serum triglyceride was at borderline high and the HDL concentration was near to the margin of low level. The TC/HDL or risk factor was considerably high (Table 3, Figure 1). There was no significant difference between fasting serum total cholesterol level, triglycerides level, HDL, LDL level and total cholesterol: HDL ratio of Group A and Group B previous to the initiation of Treatment (Table 3; Figure 1).

Table 3: Serum lipid concentrations of patients of Group A and Group B (Before Treatment).

Groups (n =	TC	TG	HDL	LDL	TC/H DL
Group A	258.6 \pm 7.0 ^a	182.8 \pm 8.2 ^a	44.2 \pm 0.7 ^a	193.4 \pm 5.8 ^a	6.5 \pm 0.2 ^a

Group B	274.2 \pm 6.0 ^a	187.8 \pm 14.4 ^a	44.5 \pm 1.4 ^a	193.4 \pm 5.8 ^a	5.9 \pm 0.2 ^a
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(In a column, data are presented as Mean \pm SEM of 20 patients per each group. In each column, data indicated by different superscript letters are significantly different from each other (ANOVA; Tukey's test: $p < 0.05$)

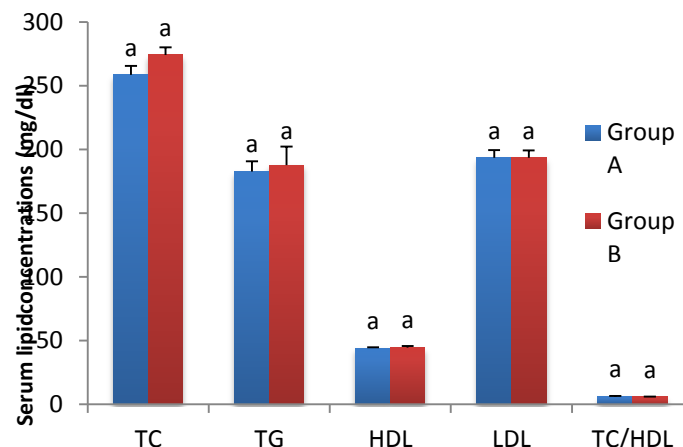


Figure 1: Serum lipid concentrations of patients of Group A and Group B (Before Treatment). (Each bar represent the Mean \pm SEM of 20 patients of each group. The bar indicated by different letters are significantly different from each other (ANOVA, Tukey's Test: $p < 0.05$))

Table 4: Lipid Profile of patients of Group A and Group B (After 14 days Treatments)

Groups (n = 20)	TC	TG	HDL	LDL	TC/H DL
Group A	208.6 \pm 7.7 ^a	129.5 \pm 7.4 ^a	47.6 \pm 0.7 ^a	175.3 \pm 9.0 ^a	4.4 \pm 0.2 ^a
Group B	250.0 \pm 6.8 ^b	183.3 \pm 13.3 ^b	45.3 \pm 1.2 ^a	185.3 \pm 6.3 ^b	5.6 \pm 0.2 ^b

(In a column, data are presented as Mean \pm SEM of 20 patients per each group. In each column, data indicated by different superscript letters are significantly different from each other (ANOVA; Tukey's test: $p < 0.05$)

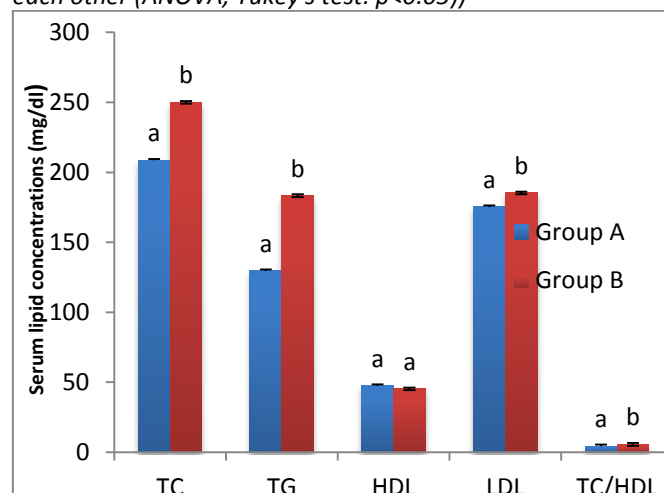


Figure 2: Lipid Profile of Group A and Group B patients (After 14 day treatments). (Each bar represents the Mean± SEM of 20 patients of each group. The bar indicated by different letters are significantly different from each other (ANOVA, Tukey's Test: $p < 0.05$)

After 14 days treatment, patients of the group A showed 19.3% decrease in serum total cholesterol level in comparison to the level of same parameter before the treatment ($p < 0.05$) whereas it showed statistically significant decrease in serum triglyceride (29%), LDL (26.5%) and TC: HDL ratio (32.3%) but the patients of group B did not show significant reduction in the serum levels of total cholesterol, triglyceride, LDL and TC: HDL ratio compared to those of before treatment of same group. The patients of group A showed significant decrease in serum concentrations of total cholesterol (16.5%), triglyceride (29.3%), LDL (5.3%) and TC/HDL ratio (21.4%) while showing considerable increase in HDL level in comparison to the serum concentrations of same lipid parameters of Group B after 14 days treatment (Table 4, Figure 2).

These results demonstrate favourable alteration in lipid profile in subjects with hyperlipidaemia during the period of oral administration of cold water extract of herbal formulation with dietary management. The lipid fraction alterations are a reflection of the summation and synergism of the individual effects of plant materials and dietary management in subjects who had an abnormal lipid profile and who continued prescribed dietary method during 14 days period in each regimen.

A 19.3% reduction was noted in total cholesterol levels of patients of group A, which received cold water extract of herbal formulation with dietary management and there was a 8.8% reduction of total cholesterol in patients treated with dietary management only (Group B). Earlier reports demonstrated 5% to 6% reduction of total cholesterol after 4 weeks of garlic supplementation alone [6]. Triglyceride level was lowered by 29.1% in this study in Group A and 2.3% reduction in group B. Previous studies with fish oil supplementation report 30% reductions in total triglycerides with low-fat diets [5]. The Group A resulted in a significant reduction of 26.5% in LDL-cholesterol and Group B resulted in 5.3% reduction in same parameter.

In the present study, there was no significant change in the HDL levels. Several studies demonstrated no effect of garlic supplementation alone on HDL [6, 7]. However, many studies with fish oil supplementation demonstrated a substantial increase in the total HDL increase (5% to 7%), particularly in low-fat diets [8]. According to above details new herbal formulation has shown a similar effect on serum level of HDL when compared with the results of other earlier studies.

The findings of earlier study with *Murryakoenigii* (Curry leaves) has shown total cholesterol (TC) decreased by 30.8%, triglycerides (TG) decreased by 37.1% and increased the HDL-cholesterol levels by 29.4% [9]. In another study with garlic reported that total cholesterol was decreased by 12.1%, LDL-cholesterol decreased by 17.3% reduction, HDL-cholesterol increased by 15.7% [10]. According to these results, the new herbal formulation of the present study has shown satisfactory efficacy in reducing the elevated serum lipid levels of hyperlipidaemic patients than the efficacy of dietary management alone.

Conclusions and Recommendations

Considering the overall results of present study and comparing with the results of previous studies, it is evident that the short term administration of cold water extract of new herbal formulation has shown significant effect in decreasing the elevated serum lipid levels (except to the HDL levels) than the effect of given dietary management alone in hyperlipidaemic patients without causing clinically evident adverse effects. The evidences revealed from this prospective cohort study provide strong scientific background for the randomized clinical trials for further evaluation.

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