Article Info

A Novel Herbal Formulation of Delstrok® for Patients with Cardiovascular Disorders

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ABSTRACT

Cases of cardiovascular disease are on the rise and demand for alternative safer methods of treatment is increasing. The study was conducted to determine the efficacy and safety of novel herbal formulation of DELSTROK® tablets in cardiovascular disease. Males and middle aged individuals showed higher risk of cardiovascular diseases. On treatment, majority of the patients showed reduction in weight and body mass index levels, as well as decreased levels of total cholesterol, low-density lipoprotein cholesterol and triglycerides. Most of the patients also showed improvement in high-density lipoprotein cholesterol levels while hs-C-reactive protein levels were lowered in all. Novel herbal formulation of DELSTROK® tablets showed protective potential towards patients suffering from cardiovascular disease. DELSTROK® tablets could be used to treat such patients and improve their quality of life.

1.0 Introduction

Cardiovascular diseases remain the leading cause of death with 20 million people dying, mainly from heart disease and stroke [1]. Cardiovascular disease (CVD) is a major cause of disability and premature death throughout the world and contributes substantially to the escalating cost of healthcare [2]. By 2030, approximately 20 % of the population above the age of 65 will be affected by cardiovascular diseases (CVD) to rank as the leading cause of death. Age can be regarded as most important determinant of cardiovascular health and the cost of treatment expected to triple [3].

Atherosclerosis is a form of cardiovascular disease caused due to blockage of arteries and plaque formation on the walls of the arteries. Cholesterol is a waxy, fat-like substance and important membrane re-inforcer made in the liver and found in body cells [4]. It is also a precursor for steroid hormones, vitamin D and bile acids [5]. Cholesterol travels in packages called lipoproteins, which have fat or lipid inside and protein outside. There are two main kinds of lipoproteins that carry cholesterol in the blood, a) low density lipoprotein or LDL that carries cholesterol to tissues, including the arteries; b) high density lipoprotein or HDL takes cholesterol from tissues to the liver, which removes it from the body. Most of the time, higher levels of LDL form of cholesterol in the blood along with lower levels of HDL indicates greater risk of heart diseases. Various risk factors contribute to unhealthy cholesterol levels that can be divided into modifiable and non-modifiable. The modifiable risk factors include issues related to diet, overweight and obesity. Non-modifiable risk factors include heredity, age and gender [4]. A study conducted on coronary heart disease patients at a hospital in Malaysia concluded that cholesterol was an important risk factor for coronary heart disease [6]. The body converts any excess calories eaten into most common fat molecule in the body called triglycerides for storage in adipose tissue. Triglycerides are then released for energy in between meals. A diet containing excess of carbohydrates and fats can lead to a condition called hypertriglyceridemia [5].

C-reactive protein (CRP) is predominantly synthesized in the liver, typically within the transcriptional phase of the response to pro-inflammatory cytokines and used as a marker for inflammation. CRP testing is not precise enough to diagnose specific diseases but serves more as a general indicator and more testing may be needed if inflammation or infection is found [7].

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Evidence suggests that CRP participates actively in the atherosclerosis process. A study conducted at Sree Balaji Medical College and Hospital (SBMC&H) Chennai concluded that presence of hs-C-reactive protein (hs-CRP) above 3 mg/L in patients can increase risk of developing coronary heart disease, thus, hs-CRP estimation can be used for screening future coronary artery disease [8].

Hypolipidemic medicines play a major role in preventing coronary artery diseases. Many hypolipidemic drugs have already proven to be useful in lowering serum lipid levels in patients. However, high costs and side effects have been reported in long term treatment process. Thus, efforts to develop effective and better hypolipidemic drugs led to the discovery of natural medicinal herbs. The beneficial uses of medicinal plants in traditional system of medicine of many cultures have been extensively documented [9].

In the era of rapid advancement in medical technology, herbal or botanical preparation commonly referred to as complementary and alternate medicine (CAM) have gained a lot of popularity in terms of healthcare maintenance in large population of developing and developed world as a source of curative and preventive remedy for various illnesses.

CAM is defined as a group of diverse practices and products in medical and health systems that are not generally considered as part of conventional medicine. Among all remedies, plants-based functional foods have gained lots of recognition throughout the world and believed to possess natural substances with potential to reduce detrimental effect of a number of cardiovascular diseases and associated risk factors. The probable reason for this rising trend is skeptic approach of general public towards conventional medicine due to fear of more side effects and increasing cost, further driven by the belief of increased safety profile and easy availability of plant-based natural products in comparison to orthodox medicine [10]. Over 80 % of the world population uses natural remedies and 70 % of doctors in Germany prescribe plant-based medicines [9].

Plants could serve as alternative sources in the development of new anticoagulant agents due to their biological activities. Scientific evidence has shown that consumption of dietary anticoagulants or phytochemicals with anticoagulant properties can ultimately reduce or eliminate the risks of

thromboembolic disease [11]. The purpose of the current study was to determine the potential of the herbal formulation of DELSTROK® tablets in lowering weight and body mass index (BMI), improving total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglyceride, high-density lipoprotein cholesterol (HDL-C) and hs-CRP levels with no harmful side effects.

2.0 Methods

2.1 Ethical clearance

Clinical trials of DELSTROK® tablet was conducted at the Department of Kayachikitsa, Bharati Vidhyapeeth, Ayurveda Hospital, Pune, Maharashtra, India after obtaining all necessary permissions and clearance from college and hospital authorities, Scientific Review Committee and Institutional Ethics Committee (Clinical IEC, Bangalore, Karnataka, India), BVDU College of Ayurved, Pune, Maharashtra, India. The study has been carried out in accordance with the Code of ethics.

2.2 Study design

An open clinical study was conducted for screening of subjects based on inclusion and exclusion criteria. The selection criteria were as follows:

2.2.1 Inclusion criteria

Individuals of either gender between 18 years to 70 years with known dyslipidemia, moderate or high CVD risk (LDL < 100 mg/dL), hypertension (blood pressure $\geq$ 140 or $\geq$ 90 mm Hg), overweight (BMI 25.0-29.9 kg/m^2) and obesity (BMI $\geq$ 30 kg/m^2), pre-diabetic (fasting plasma glucose >110 mg/dL) and diabetic patients.

2.2.2 Exclusion criteria

Age below 18 years and above 70 years, medical history of unstable angina, acute coronary syndrome, myocardial infarction, heart failure or stroke within three months of the study, uncontrolled hypertension (diastolic blood pressure > 100 mmHg), type 1 diabetes mellitus and uncontrolled diabetes (fasting blood glucose $\geq$ 200 mg/dL) with emergencies, history of cerebrovascular accident with neurological complications, bronchial asthma or chronic obstructive pulmonary disease and any other major

respiratory diseases, impaired renal function (creatinine ≥ 2.0 mg/dL), chronic kidney disease and renal disorders, peptic ulcer with bleed, or bleeding diathesis; pregnant or lactating mothers; patients taking any ayurvedic drugs and/or experimental drug during the last twenty five days for the same reason.

2.3 Assessment criteria and parameters

Counseling and informed consent of selected subjects was conducted. Initial assessment of weight, BMI, total cholesterol, LDL-C, triglycerides, HDL-C and hs-CRP levels was carried out. The expected primary outcome of the study should be improvement in lipid profile, weight and BMI, hs-CRP and CVD risk factor modifications while the secondary outcome can be associated with patients being prioritized to receive preventive treatment to reduce CVD risk. DELSTROK® 700 mg tablet were orally administered to each patient twice a day (morning and evening) along with lukewarm water after meals for three months. Intermediate follow-ups were carried out every fifteen days wherein patients underwent clinical examination during treatment. At the end of the study the patients were observed for changes in body weight, BMI, total cholesterol levels, LDL-C levels, triglycerides levels, HDL-C levels and hs-CRP levels. The data of the clinical study performed on the enrolled patients (Table 1) distributed based on age and gender. Overall assessment of parameters was estimated as follows- a) above 75 % improvement: marked effect; b) 50 %-75 % improvement: moderate effect; c) 25 %-50 % improvement: mild effect and d) below 25 % improvement: no effect.

3.0 Results

Males and middle aged individuals showed higher risk of cardiovascular disease (Figure 1). On treatment, majority of the patients showed reduction in weight and BMI levels (Figure 2); decreased levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C) and triglyceride levels (Figure 3). Out of 10 patients, 6 showed HDL-C levels >10 mg/dL, 3 patients showed no change in levels while 1 patient showed a decrease in HDL-C levels. Out of 10 patients, 8 patients showed lowered hs-CRP levels compared to pre-trial levels in the range from 0.12 mg/L to 0.2 mg/L; 2 patients with pre-trial levels 0.16 mg/dL and 0.12 mg/dL showed an increase in

hs-CRP level of 5.95 mg/L and 0.18 mg/L, respectively. This elevation might be associated with a non-specific inflammatory process as the patient had history of viral fever 15 days prior to the blood investigation. However on evaluation after three months, hs-CRP level decreased.
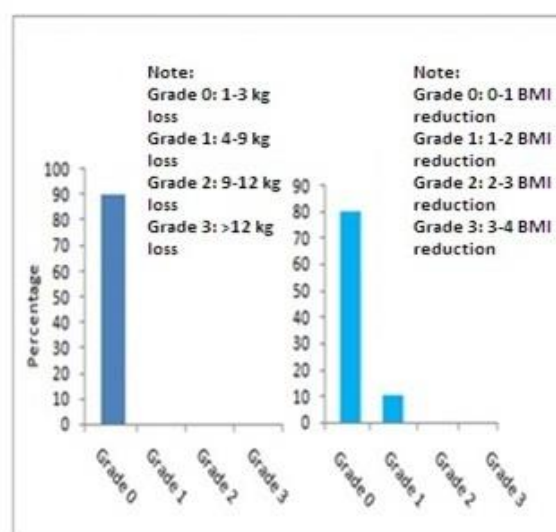
**Table 1: Data of Patients Enrolled for Clinical Trials**

Details	Group
No. of patients enrolled	14
No. of patients (taken complete treatment)	10
No. of patients (dropped out)	02
No. of patients (ongoing treatment)	02

Figure 1: Percentage Distribution of Patients Based on Age and Gender
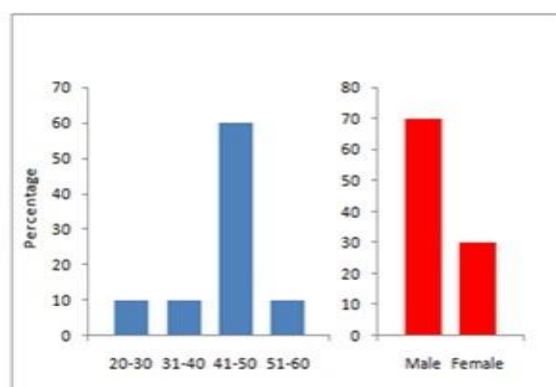
Figure 2: Effect of DELSTROK® on Body Weight and Body Mass Index of Patients

Fig. 3: Effect of DELSTROK® on Lipid Profile of Patients
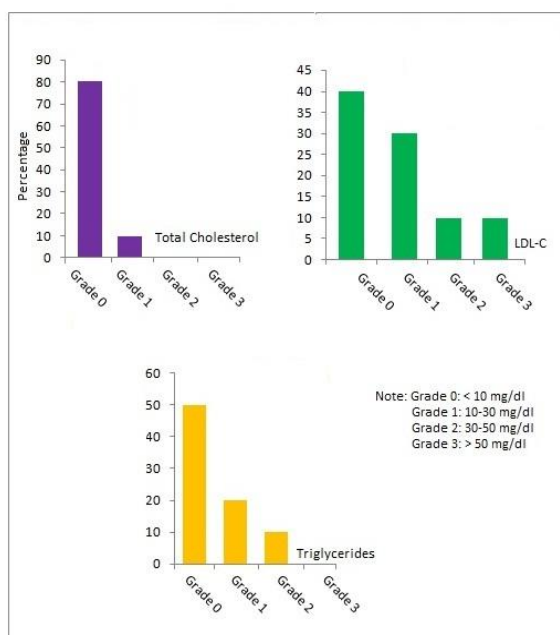
4.0 Discussions

Cardiovascular disease develops 7 to 10 years later in women than in men and considered a major cause of death in women over the age of 65 years [3]. In the present study, majority of the patients were males and belonged to age group of 41-50 years. This finding is similar to a follow up study on 14786 middle-aged men and women in Finland carried out by Pekka J. et al that found coronary heart disease incidence three times higher in middle aged men than women [12]. Weight loss of 1-3 kg was prominent and BMI was lowered in majority of the treated patients. Reduction in weight in the present study could be attributed to the formulation administered similar to previous studies carried out by Satish et al [13] using 90 obese individuals and Amtia et al involving 100 obese middle aged women as subjects [14]. For the parameter of total cholesterol in the current study, majority of the patients showed reduction in cholesterol level and LDL-C that could be attributed to the constituents present in DELSTROK® tablets. Also, in the current study, fifty percent of the patients were found to have lowered triglyceride levels while HDL-C in most of the patients was increased. In a previous study on 112 hyperlipidemic patients carried out by Negar et al [15], Allium sativum in combination with juice of

Citrus limon reduced total cholesterol and LDL-C levels. Additionally, Zingiber officinale was found to significantly lower LDL-C and serum cholesterol levels as reported by Shah et al in a study conducted on 30 hyperlipidemic patients [9]. Prior studies conducted by Satish et al [13] found honey to lower total cholesterol, LDL-C and triglyceride levels while increasing HDL-C levels in obese subjects. Additionally, according to a review by Qidwai et al. [10] various studies conducted have found Allium sativum to reduce triglyceride levels. A double blind controlled clinical trial conducted by Alizadeh-Navaei et al [16] found that the group treated with Zingiber officinale showed reduction in LDL levels and increase in HDL levels compared to the placebo group.

In the present study, hs-CRP levels were lowered similar to effect of extract of Zingiber officinale in lowering CRP levels as well as total cholesterol and triglyceride levels as reported by Arablou et al [17] in a clinical trial of 70 patients with type-2 diabetes. Garlic supplementation reduced serum concentrations of CRP in a randomized clinical trials conducted by Mofrad MD et al [18]. In the present study, DELSTROK® tablets were concluded to have protective potential in lowering weight and BMI, improving the lipid profile and hs-CRP levels. Studies carried out by Warshafsky and colleagues deduced that hypercholestrolemic patients treated with Allium sativum that of patients treated with a placebo [19]. Additionally, studies carried out by Adler et al found that garlic was effective in reducing serum cholesterol levels wherein the average drop in total cholesterol was 9.9 %, LDL 11.4 %, and triglycerides 9.9 % [20]. A clinical trial conducted showed honey had mild reduction in body weight, fat weight and body fat percentage along with significantly decreased BMI [21]. Another study found significant reduction in serum CRP concentrations following ginger supplementation [22]. No adverse effects were observed in the patients in the present study, contrary to fewer side effects reported in clinical studies using garlic and its preparations [23]. This supports the inclination of general public towards conventional medicine due to fear of more side effects and high cost, increased safety profile and easy availability of plant-based natural products in comparison to orthodox medicine has been observed had 9 % lower mean plasma cholesterol concentration than

5.0 Conclusions

DELSTROK® tablet given along with lukewarm water after meals i.e. morning and evening for three months showed decrease in weight, BMI, total cholesterol, LDL-C and triglyceride levels. There was mild improvement in HDL-C levels and decrease in the hs-CRP levels. This study showed significant protective potential of DELSTROK® in cardiovascular disorders and no adverse drug effects were found during the trial.

6.0 Acknowledgment

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