

Spirulina and Herbal Combination on Metabolic Alterations of Cardiovascular Diseases (CVDs)

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ABSTRACT

Cardiovascular diseases (CVD) and metabolic changes are among the foremost public health concerns that have been accounted in people alive with cardio infections. Issues contributing to heart metabolic condition in CVD take in body fat allocation, dyslipidemia, insulin conflict, cardiovascular dysfunction and swelling. CVD have appeared as a main public health trouble and impose a rising load on the health care system. Increased coronary heart disease risk and conventional risk issues contribute to elevate the risk. They stay the foremost roots of morbidity and mortality globally. The employ of medicinal herbs keeps on to be an alternative action move toward for some infections including CVDs. Presently, there is an unprecedented constrain for use of herbal preparations in current medicinal systems. This drive is powered through several aspects that are cost-effective therapeutic assure contrast to standard therapies with safety. Consequently, public awareness should be raised about medicinal herbs, toxicity, potentially life threatening, and possible herb-drug interactions.

Present article highlighted the significant effect of *Spirulina* and other herbs supplementation individual and in combination. Many attempts on medicinal herbs in order to use in CVD treatments were reported. We overview the use of these herbs having ethno pharmacological curative potentials and medicinal properties against CVDs are reviewed. The employment of a range of herbs in the context of CVDs, such as myocardial infarction, hypertension, peripheral vascular diseases, coronary heart disease,

cardiomyopathies, and dyslipidemias has been reviewed, analyzed, and significantly discussed.

Key Words: Spirulina, herbal medicine, cardiovascular diseases, atherosclerosis, hypertension, medicinal plants, antioxidants, oxidative stress.

INTRODUCTION

Major public health problem like cardiovascular diseases (CVD) have emerged and impose an escalating burden on the health care system in India. The World Health Organization (WHO) reported that CVDs account for 30% of global deaths annually ^[1]. In Europe, CVDs account for 45% of all deaths according to the European Cardiovascular Disease Statistics 2017 ^[2]. The American Heart Association's current statistics estimate that around 50% population of USA has a form of CVD ^[3].

CVDs are a variety of ailments counting peripheral vascular diseases, coronary heart disease (CHD), heart failure, myocardial infarction, stroke, hypertension, cardiomyopathies, and dyslipidemias, among others ^[4,5]. Frequent risk issues for CVDs contain smoking, harmful diet, diabetes mellitus, hyperlipidemia, raised levels of low-density lipoprotein cholesterol (LDL), repressed levels of high-density lipoprotein cholesterol (HDL), and hypertension ^[1]. Some risk issues for CVDs direct to endothelial cell dysfunction, which has been associated as an input occurrence in the atherosclerosis pathogenesis,

coronary vasoconstriction, and, possibly, myocardial ischemia. Augmented coronary heart disease (CHD) risk contributes to elevate the threat [1]. Some common CVDs risk issues, such as diabetes, hypertension, can influence to CVDs by means of the mediation of inflammation [6-8].

Studies accounted an increase of triglycerides (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), and diminish of high density lipoprotein cholesterol (HDL-C) has lift up concerning increased atherogenesis risk and atherosclerotic vascular illness [9-12]. Current statements have shown that cardiovascular deaths explanation for 6% of entirety deaths in a large observational. CVDs have been the leading reason of morbidity and mortality in the general population and have nowadays also been distinguish as a major death cause [3]. Atherosclerosis is risk issue, also major CVD incidence contributor. Around 50% of deaths in developed countries are because of atherosclerosis [13,14]. High BP expresses the hypertension referred to CVD and involve as major risk factor and donor to additional CVDs and other ailments. Independent predisposing issue hypertension responsible for retinopathy, nephropathy, heart failure, coronary artery disease, stroke, and peripheral arterial diseases [15,16].

High mortality and morbidity correlated with these diseases [17]. In addition, hypertension is the particular most important risk factor for atherosclerosis, and any clinical ending of atherosclerosis. Silent killer (Hypertension) does not illustrate indications until afterward disease periods [15]. Since of this, it is not surprising that hypertension influences 1.2 billion people and explanations for about 9 million deaths yearly [18,19]. As a result, recently there has been main enforcement on CVD avoidance [20]. Consequently, new treatment choices are urgently demanded for types of CVDs, allowing for the persisted burden stemming from CVDs is at rest substantial.

HERBAL AND PLANT PRODUCTS AGAINST CVD

Herbs, defined as form of plant or plant product and plant extracts appear the basis of initial drugs employed in established medicine systems of civilizations or cultures [21]. Plants and herbs have always been a frequent source of medications, moreover in the outline of extracts or as pure active compounds [22]. WHO estimated that approximately 60% of the world population frequently depended on plant-derived medicines [23]. Although the several achievements of by means of natural products for drug creation, advances in combinatorial action focus on drug finding attempts from natural products synthesized at the laboratory.

This is mostly since natural product-based a complex drug discovery and development endeavor requiring costly and elevated incorporated interdisciplinary approaches [24]. However, at present the use of natural products as drugs or as drug discovery platforms is well and alive [25]. In actual fact, herbal and plant-derived extracts are becoming key stream as advances in scientific research are viewing their magnitude in the prevention and treatment of diseases. However, modern scientific evidence, technical advances, clearly pointed that naturally-derived compounds will be most important foundations of new drugs [26]. Therapeutic applications of herbal and plant remedies are not only inexpensive, except they also enclose several bioactive components [27]. An additional cause intended for the regained interest in medicinal plant products is that, in their efforts to control diseases amid scarce socioeconomic sources, rural communities in budding countries have establish resort in herbal and plant obtained remedies. This is owing to several factors, but in particular to the fact that plant-based medicines are a cheaper option with fewer side effects [28].

Additionally, since herbs are examined as food creations, they are not issue to the identical observation and directive as conformist drugs [21].

Furthermore, herbal remedies are out looked by patients as organism normal and therefore safe. Natural creations commonly demonstrate adverse toxicities and pharmacokinetics, restraining their clinical prospective [29]. Generally, natural products have been the single most creative drug source leads still though small of nature's biodiversity has been tested in favor of biological commotion yet [30]. Present health care guidelines emphasize avoidance to diminish the CVDs [31]. This is carried out via addressing the chief CVD risk causes and demanding to reduce their undesirable results.

CLINICAL TRIALS OF VARIOUS HERBS AGAINST CVD

Clinical examinations have clearly exposed that such therapies are efficient in lowering CVD risk [31]. Herbal remedies enclose abundant bioactive and thus, have multi-modal cellular mechanisms of action. In fact, herbal therapies can have anti-proliferative antioxidant, vasorelaxant, anti-inflammatory, and diuretic consequences. Herbal therapies can also put off VSMC phenotypic switching; inhibit platelet activation, endothelial dysfunction, macrophage atherogenicity, lipid peroxidation, and ROS production. Because of such an extensive variety of molecular and cellular targets, herbal groundings can be used to treat and direct a range of CVDs. *S. miltiorrhiza* extracts have shown strong antioxidant capabilities with a high aptitude to search free radicals, which appears and support to its cardio and vascular-protective strong potential [32]. *S. miltiorrhiza*, contains Astragaloside IV, which is the major bioactive composite extensively employed as antioxidant and for protection against ischemic-associated CVDs [33]. Danshen plant rhizome utilized for active compounds, these bioactive compounds are the lipo-soluble (Tanshinones) and the water-soluble Phenolics [34, 35].

Numerous clinical trials have been carried out to evaluate the cardio-protective and valuable outcomes of Ginseng and its

elements in CVD action. Ginseng and its ginsenoside ingredients have vasorelaxation, anti-inflammation, and anti-oxidation, activities [36, 37]. Red Ginseng supplementation get betters lipid profiles through retreating the cholesterol, triglycerides total plasma levels, LDL-C, free fatty acids, and platelet adhesiveness and increasing HDL-C in humans and rats total plasma [38]. A significant number of clinical trials deal with CVDs. Hypertension covered eight trials, five addressed arterial occlusive illness, and an additional five deal with strokes. One such scientific trial inspected the vasorelaxation results of Ginseng and its capability to modulate vascular purpose. Trial contributors were randomized to the selected Ginseng extract or placebo groups as well as accepted 3g of Ginseng as daily dose for 12 weeks in combination with their standard antihypertensive and anti-diabetic treatment.

Allium sativum (Garlic) is a characteristic example of herbs employed in CVDs organization and is moderately recognized for its multifaceted properties next to CVD-connected states such as hypertension, oxidative stress, inflammation, and hyperlipidemia [39,40]. Certainly, through dropping TC and LDL levels, declining the contented of lipid in arterial cells and inhibiting VSMCs increase, garlic can be employed to direct atherosclerosis and hyperlipidemia [41]. An additional herb, *Crocus sativus*, can obstruct Ca²⁺ channels via endothelium-independent means provided that another vasodilator mechanism, in addition to its eNOS activating ability [42]. Although herbs have been extensively employed in both conventional and modern medicine, number of assessments that gather them and widely focus on their mechanisms of action and protection in the context of CVDs are present. Plant-based composites come out to have cardiovascular defensive outcomes; nevertheless, amongst the most efficient compounds are saponins, polysaccharides, flavonoids, and terpenoids,

SPIRULINA EFFECT AGAINST CVD, LIPID PROFILE AND ATHEROGENIC INDEX

This blue green alga is used as a food supplement all over the world [43,44]. Several findings associated concern to cholesterol reduction and balance of metabolism [45-49]. Studies have displayed its valuable effects on human health on lipid metabolism, glucose, and blood pressure during its full content in antioxidant merged with vitamin A, B12, proteins and mineral salt and also in building immunity of subjects and numerous cardiovascular risk features [50-53]. The protein C-phycoerythrin present in *Spirulina* play a critical function in the hypercholesterolemia declinement [54,55]. Animals who consumed *Spirulina* there is a significant increase in lipid profile HDL-C and reduce in TC, LDL-C and TC. Change in the CT/HDL-C ratio atherogenic index by means of the substitutable by LDL-C/HDL-C and the TC/HDL reduced considerably in the *Spirulina* administrated animal.

The TG, TC and LDL-C concentration considerably decreased in the *Spirulina* group even as those of the control group increased. The lipid profile which contains the TG, TC, HDL-C, LDL-C and the atherogenic index were determined. This result highlighted that the consumption of *Spirulina* significantly maintained the lipids profile. The levels of TG of patient from *Spirulina* group, initially higher than those of control group appreciably dropped at the end of the administration. The HDL-C levels increased considerably at same observational findings. The atherogenic index LDL-C/HDL-C results showed notably decreased after one year. These results reveal that *Spirulina* supplementation on diet have benefit impact on the lipid profile of CVD cases. It is important to note that even as some nutritional supplements can negatively interrelate with recommendation medications some supplements might also have positive impacts on CVD [56]. The *Spirulina* supplementation in diet improves the living

situations of CVD subjects through balancing macronutrients and that's express an imperative function on the patient's health. Dyslipidemia also balance cure through the *Spirulina* consumption, it is one of the major changeable risk causes of CVD. The dyslipidemia is distinguished through reduce of levels of HDL-C, and an increase of the levels of LDL-C and triglycerides elevated levels (TG). In the initial state, study demonstrated that TC, LDL-C and TG level was lesser in the control group compare to the *Spirulina* administration group.

Subsequent to six months, the points of TC, LDL-C in the serum were elevated in the control group contrast to the *Spirulina* supplementing group of subjects. The concentration of HDL-C increased throughout the same period. The cholesterol levels increase, in particular LDL-C, TG and TC in the control group put forward the trouble in the lipids metabolism which can be characteristic to the malnutrition [56]. *Spirulina* positively influence the dyslipidemia from side to side the inversion of lipid profile in the group getting *Spirulina*. The increase TG level in the serum most likely caused through an increase of VLDL levels has formerly been found to be association to an increase in the fusion of hepatic fatty acids. In separate study, TC was considerably lower in patients who received *Spirulina* as supplement by means of a considerably elevated HDL-C concentration in the same group during end of the trial. The HDL-C level elevation occurs previous to hypertriglyceridemia, associates with other findings which exhibited that supplementation of diet with *Spirulina*. Decreases LDL-C and increases HDL-C with a possible valuable outcome [53]. Explorations on the results of lowering blood cholesterol via *Spirulina* in rats [54,55] and in dissimilar doses 5-16% of diet have been issue [55]. Finding exhibited that any infection induces an increase the level of TG, LDL-C, TC and the decline HDL-C in accordance of other observation [56,57]. The

examined variation of cholesterol metabolism in CVD subjects may be elucidated through lipid per oxidation^[58,59].

The alteration of cholesterol metabolism observed in patients possibly give detailed through the augment of lipid peroxidation via exciting the of reactive oxygen species creation^[60,61]. The mechanism employed through *Spirulina* to decrease the hypercholesterolemia and lipid disorders have not so far explained even though some researchers suggested that the addition of this alga in the diet decline the intestinal cholesterol absorption and re-absorption of bile acids in the ileum^[62,63]. Consequently, the *Spirulina* can be believed a functional food capable of cholesterol levels reduction and as a result preventing atherosclerosis.

Hypercholesterolemia was induced in rabbits by feeding them a high cholesterol diet and the outcomes of supplementing this diet with 0.5g/d *Spirulina* was assessed by means of measuring the serum TC, TAG and HDL-cholesterol level at the begin of the testing and following 30 d and 60 d. It was originate that the levels of serum cholesterol reduced from 1,054±100 mg.dL⁻¹ in the rabbits fed a cholesterol diet without *Spirulina* to 510±160 mg.dL⁻¹ to those fed with a high cholesterol diet supplemented with *Spirulina*^[64,65]. The addition of *Spirulina* to the cholesterolemic diet did not reason significant reducing the of triacylglycerols levels.

ANTIOXIDANT MECHANISM OF *SPIRULINA* DURING CVDS

Spirulina microalgae are potential nutrient food and supplement^[66]. The antioxidant mechanism of *Spirulina* can also be put forwarded caused by the protein C-phycocyanin presence; their structure is closed like bilirubin which plays a significant physiological position beside reactive oxygen species^[67]. This C-phycocyanin protein inhibits oxidative transforms in plasma aromatic amino acid residues and proteins^[68], lipoprotein lipase enzyme, is a key enzyme in the ileum

metabolism^[69]. Therefore, they suggest that *Spirulina* can be believed a useful food capable of reducing the levels of cholesterol and following preventing atherosclerosis. The antioxidant mechanism of *Spirulina* can also be put forwarded due to C-phycocyanin protein occurrence like, to be bilirubin express an essential physiological point^[70]. Complete cardiovascular risk factors were reviewed in this study. However, the reduced cardiovascular diseases risk associated with *Spirulina* intake is well recognized^[71], additional factors not regulated in the examination were the mechanisms of *Spirulina* on lipoprotein lipase which may have influenced the diminished of triglycerides.

The occurrence of antioxidant compounds (phycocyanin and phenolic compounds, and poly-unsaturated fatty acids) in the *Spirulina* can be the reason of the *Spirulina* properties on the reducing of serum lipids stages. According to Nagaoka et al. (2005)^[72], both, *Spirulina* concentrates or phycocyanin, a proteic pigment *Spirulina* extract, caused hypocholesterolemic activity in rats. The in vivo antioxidant ability of *Spirulina* extracts was estimated through Miranda et al. (1998)^[73] in plasma of Wistar rats getting 5 mg extract for 2 and 7 weeks daily. Consequently, it could be concluded that 0.5g.d⁻¹ of *Spirulina* supplementing grounds a diminish in the induced hypercholesterolemia in rabbits. The serum cholesterol levels diminished in the rabbits fed a hypercholesterolemic diet without *Spirulina* in contrast to those fed a hypercholesterolemic diet administrated with *Spirulina*. In contrast, the serum HDL level was elevated in the groups feed with *Spirulina*. Results demonstrated the *Spirulina* potential to reduce the TC serum levels and to increase the HDL-C, regard as a protective factor next to the progress of atherosclerosis.

Plasma antioxidant capability was determined in brain homogenate keep alive for 1h at 37°C. During treatment, the plasma antioxidant capacity was 71% for the experimental group and for the control

group 54%. The authors believed that the quantity of phenolic acids, a-tocopherol and b-carotene presents in *Spirulina* extracts were accountable via the antioxidant action. The *Spirulina* having poly-unsaturated fatty acids as revealed through many authors [74-78]. These compounds have been considered in respect to its beneficial properties such as its aptitude to decline blood cholesterol levels [79,80].

CONCLUSION

Even though the abundance of information regarding CVDs, occurrence of CVDs carries on to be on the rise of lipid profile along with metabolic changes. Thus, there is direct demand for new safe, efficient, and moderately cheap drug. Rising confirmation obtained from in vitro and in vivo studies put forwards that the medicinal plants discussed in this review considerably modulate key cellular, molecular, and metabolic mechanisms that control CVDs pathogenesis and pathophysiology, similarly the nutritional supplement *Spirulina* combined with a quantitative and qualitative balanced diet for at least six months can slow down an exposition to lipid abnormalities in CVD. Additional studies are suggested on a large group of animals exposed to CVDs risk factors. Here are presented findings, go forwards, and studies relating the beneficial assessments of herbs in the context of CVDs. Current proof reveals that a variety of herbs and *Spirulina* have potent therapeutic properties and can improve pathological states correlated with CVDs.

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