

A Review on Nutraceuticals and Diet in Prevention of Cardiovascular Diseases

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ABSTRACT

Nutraceuticals and diet are very important for prevention of cardiovascular diseases. CVD has become important public health problem over the last few decades. The patients are much aware of the side effects, contraindications caused due to the chemical agents in short and long term therapy. Thus the interest to prevent medicine from every small disease came into trend and consequently led to new research on alternative therapies preferably with the help of nutritional approaches. Nutraceuticals have received considerable interest because of their presumed safety and potential nutritional and therapeutic effects. This review gives highlights of some important facts regarding therapeutic use of nutraceuticals and diet in prevention of CAD. Novel dietary approaches to cardiovascular prevention are of major significance in clinical research and practice thus advances in the knowledge of both the disease processes and healthy dietary components have provided new avenues to develop dietary strategies to prevent CVD.

Keywords: Nutraceuticals, Diet, Cardiovascular diseases.

INTRODUCTION

The term nutraceutical was coined from nutrition and pharmaceutical in 1989 by Stephen DeFelice MD, founder and chairman of the foundation for Innovation in Medicine (FIM), Cranford, NJ. According to WHO, about three-quarters of the world population depends upon traditional remedies for the health care of its people. Infact, herbs and nutraceuticals are the friends of human being. They not only provided the food and shelter but also serve the humanity to cure different dysfunctions.¹ Over the last 20 years, numbers of Nutraceuticals are available for self-medication or for sale.² "Nutraceutical" is a marketing term developed for nutritional supplement that is sold with the intent to treat or prevent disease and thus has no regulatory definition.³ Hence a "nutraceutical" is any substance that may be considered a food or part of a food and provides medical or health benefits, encompassing, prevention and treatment of diseases. Such products may range from isolated nutrients, dietary supplements and diets to genetically engineered "designer" foods. Presently over 470 nutraceutical and functional food products are available with documented health benefits.⁴

Concept of Nutraceuticals.⁵



Scientific and technologic developments are increasing the possibilities of modifying traditional foods and developing new food sources to meet these newly discovered requirements. Using modern genetics, chemistry and molecular biology, the scientific community is now able to design and manufacture foods having specific characteristics.⁶ The scope of nutraceuticals is significantly different from functional food for several reasons. These include: (i) Prevention and treatment of disease

(i.e., medical claims) are relevant to nutraceuticals, but only reduction of disease, not the prevention and treatment of disease, is involved with functional foods. (ii) Nutraceuticals include dietary supplements sold in forms that are similar to drugs: pills, extracts, tablets, etc as well as other type of foods, functional foods must be in the form of ordinary food.^{7,8} The term "bioactive foods" was first defined as "foods, food ingredients or dietary supplements that demonstrate specific health or medical benefits including the prevention and treatment of disease beyond basic nutritional functions". Now bioactive foods and Nutraceutical have emerged as potential supplements in cardiovascular and cancer preventive natural sources from food.⁹ A successful bioactive food product's bioactive role needs its perceptible health benefit. If a health benefit is clearly understandable, or if the health benefit is clearly perceptible such as weight loss or stress reduction, or can be easily measured - such as a product that reduces cholesterol, then the product is much more likely to succeed. Now interest is growing for use of bioactive foods in cardiovascular prevention. Recently JIVA™ a bioactive food made of resveratrol combined with garlic has been advocated as potential cardiovascular prevention formula.¹⁰

Cardiovascular diseases (CVD) is the name for the group of disorders of the heart and blood vessels and include hypertension (high blood pressure), coronary heart disease (heart attack), cerebrovascular disease (stroke), heart failure, peripheral vascular disease, etc. In 1999 CVD alone contributed to a third of global deaths and by 2010 it would be the leading cause of death in developing countries. Majority of the CVD are preventable and controllable. It was reported that low intake of fruits and vegetables is associated with a high mortality in cardiovascular disease.^{11,12} Many research studies have identified a protective role for a diet rich in fruits and vegetables against CVD.¹³ This apart, nutraceuticals in the form of antioxidants, dietary fibers, omega-3 polyunsaturated fatty acids (n-3 PUFAs), vitamins, and minerals are recommended together with physical exercise for prevention and treatment of CVD. It has been demonstrated that the molecules like polyphenols present in grapes and in wine alter cellular metabolism and signaling, which is consistent with reducing arterial disease.¹⁴

It is now evident, based on the extensive scientific evidence, that functional foods have broad ranging physiologic effects in vivo that lessen inflammatory cascades and vascular

reactivity. Nutrition is a very complex research topic and it is not clear whether an individual component of the diet or a combination of nutrients and dietary habits may be responsible for any cardioprotective effects.

1. BACKGROUND INFORMATION OF CARDIOVASCULAR DISEASES

The worldwide prevalence of cardiovascular risk factors is increasing. Hypertension, which was identified in a recent World Health Organization report as among the most important preventable causes of premature death, affected 972 million people worldwide in 2000 and is predicted to increase by around 60% to 1.56 billion people by 2025.¹⁵ Similarly, diabetes, which currently affects 151 million people globally, is expected to increase by 46% to 22 million by 2010.¹⁶ Global risk assessment can identify both the high-risk patients who need aggressive intervention, as well as patients who might appear to be at low risk but who are actually at a much higher risk of CVD.¹⁷ CVD nevertheless remains the main cause of death, especially ischemic heart disease and cerebrovascular disease (CD).¹⁸⁻²⁰ The origin of these diseases is multifactorial, but cardiovascular risk factors (CVRF) represent some of the most important causes. Of importance among CVRF are age and sex, as unmodifiable CVRF, and smoking, high blood pressure, hypercholesterolemia, and diabetes mellitus (DM) as modifiable CVRF.²¹ Recently, other CVRF, such as hypertriglyceridemia,²² of all-cause, coronary heart disease, and stroke mortality.²³⁻²⁷

2. DEFINITION OF NUTRACEUTICALS

About 2000 years ago, Hippocrates correctly emphasized "Let food be your medicine and medicine be your food". Currently there is an increased global interest due to the recognition that "nutraceuticals" play a major role in health enhancement. The term "Nutraceutical" was first coined by Dr. Stephen L. Defelice as "a product isolated or purified from foods and sold in medicinal forms. They have physiological benefit" Nutraceutical is a combination of 2 words

1. Nutrition and 2. Pharmaceutical.

Nutraceuticals are food product that provides health as well as medical benefits; including the prevention and treatment of disease. Phytochemicals and antioxidants are two specific types of nutraceuticals. Research has

proved that foods with phytochemicals may help to provide protection from diseases such as cancer, diabetes, heart disease, and hypertension, e.g. carotenoids found in carrots. Antioxidants may be helpful in avoiding chronic diseases, by preventing oxidative damage in our body.²⁸

3. CATEGORIES OF NUTRACEUTICALS²⁹

Nutraceuticals are non-specific biological therapies used to promote wellness, prevent malignant processes and control symptoms. They are categorized as follows.

3.1. Based on chemical constituents

(a) Nutrients³⁰

Substances with established nutritional functions, such as vitamins, minerals, amino acids and fatty acids.

(b) Herbals³¹

Herbs or botanical products as concentrates and extracts.

(c) Dietary Supplement

Dietary supplements are products administered through mouth that contain a dietary ingredient intended to add something to the foods you eat. Examples of dietary supplements are black cohosh for menopausal symptoms, ginkgobiloba for memory loss, and glucosamine/chondroitin for arthritis. They also serve specific functions such as sports nutrition, weight-loss supplements and meal replacements. Supplement ingredients may contain vitamins, minerals, herbs or other botanicals, amino acids, enzymes, organ tissues, gland extracts, or other dietary substances. They are available in different dosage forms, including tablets, capsules, liquids, powders, extracts, and concentrates.³²

3.2. Traditional and Non- Traditional nutraceuticals

Wide variety of nutraceutical foods are available in the market which falls in the category of traditional foods and non-traditional foods.

(a) Traditional Nutraceuticals

Under the category of traditional Nutraceuticals comes food in which no change to the food are made; it is simply natural, whole foods with new information about their potential health qualities. There has been no change to the actual foods other than the way the consumer perceives them. Many fruits, vegetables, grains,

fish, dairy and meat products contain several natural components that deliver benefits beyond basic nutrition, such as lycopene in tomatoes, omega-3 fatty acids in salmon or saponins in soy. Even tea and chocolate have been noted in some studies to contain health-benefiting attributes. Tomatoes and salmon are two types of food that researchers have found to contain benefits beyond basic nutrition - in this case, lycopene and omega-3 fatty acids, respectively.

(b) Nontraditional Nutraceuticals

They are the outcome from agricultural breeding or added nutrients and/or ingredients such as orange juice fortified with calcium, cereals with added vitamins or minerals and flour with added folic acid are nontraditional nutraceutical. Agricultural scientists successfully have come up with the techniques to boost the nutritional content of certain crops. Research currently is being conducted to improve the nutritional quality of many other crops.³³

4. Role of nutraceuticals and diet in the prevention of CVD

4.1. The Protective Effect of Diet in CVD

It has been proposed that CVD can be prevented by lifestyle changes, including diet.³⁴ Early evidence for the role of diet on CVD came from data on trends in food consumption, and ecological studies have shown associations between CVD prevalence and fat intake.³⁵ Moreover, excessive consumption of foods that are caloric dense, nutritionally poor, highly processed, and rapidly absorbable can lead to systemic inflammation, reduced insulin sensitivity, and a cluster of metabolic abnormalities, including obesity, hypertension, dyslipidemia, and glucose intolerance.³⁶ An integrated approach combining lifestyle modification with the correct pharmacologic treatment is sought to reduce cardiovascular risk factors, to improve vascular health, and to reduce healthcare expenditure.³⁷ The conflicting results between the apparent protective effects of nutrients as part of dietary intake and the lack of effectiveness of single nutrient supplementation in trials has led to a focus on whole foods or modified diets as protective against CVD.³⁸

4.2. Some Dietary Patterns and Reduced Risk of Cardiovascular diseases

Eating habits and dietary trends have health, environmental, and social impacts. Some diet

plans demonstrated the ability to reduce cardiovascular risk.³⁹

4.2.1. Mediterranean Diet.

The Mediterranean diets contain high levels of fruits, vegetables, cereals, beans, nuts and seeds, and olive oil, with little red meat and dairy products. Fish and poultry are consumed in low-to moderate amounts; and wine is consumed in moderation. They have received great attention and numerous reports have demonstrated low rates of chronic disease among populations known to consume these diets.⁴⁰ Moreover, clinical trials have confirmed their cardiovascular protective effects and their effectiveness to reduce inflammatory markers in high-risk populations.⁴¹⁻⁴³ Several Mediterranean diet foods, including polyunsaturated fat products, vegetables, fruit, whole grains, legumes, and low glycaemic index starchy foods with functional properties may protect against type 2 diabetes.⁴⁴ They were also shown to reduce serum homocysteine concentrations and consequently the risk of coronary events, especially in high-risk individuals.⁴⁵ Olive oil (which induces a high ratio of monounsaturated to saturated lipids) appears to be chiefly responsible for the apparent protection offered by the Mediterranean diet against hypertension.⁴⁶ The high antioxidant content of plant foods and olive oil may also contribute to the health of the vascular system. However, it has been indicated in a recent review that not all components of the Mediterranean diet are equally protective⁴⁷ and homocysteine.⁴⁸ As a whole, the evidence for the protective role of the DASH dietary pattern in prevention of CVD is strong.

4.2.2. Portfolio Diet.

Step I and Step II diets are early examples of dietary strategies recommended for the clinical management of high blood cholesterol.⁴⁹ The Step I diet requires a total fat intake of less than 30% of total calories, with saturated fatty acids contributing to less than 10% of total calories and cholesterol less than 300 mg/day. For individuals who require a more aggressive approach to meet their LDL-C goals, the Step II diet, which lowers saturated fatty acids to less than 7% of total calories and cholesterol to less than 200 mg/day, is recommended. Current recommendations for CVD risk reduction continue to focus on LDL-C as a major therapeutic target. The National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III guidelines recommend

therapeutic lifestyle changes for individuals whose LDL-C levels are above goal (2001). LDL-C lowering can also be achieved by adding other dietary components, specifically plant sterols, viscous fibers, soy protein, and almonds. This combination of dietary components has been labeled the Portfolio diet.⁵⁰ Another important attribute of the Portfolio diet is its beneficial effects on C-reactive protein lowering, a strong independent predictor of cardiovascular risk.⁵¹

4.2.3. Vegetarian Diet.

A vegetarian diet, devoid of meat and fish, and high in fruits, vegetables, and nuts, rich sources of the antioxidant nutrients and polyphenols, contribute to the anti-inflammatory potential of these diets. In terms of micronutrients content, vegan diets are usually higher in magnesium, folic acid, vitamins C and E, iron, and phytochemicals, and they tend to be lower in n-3 fatty acids, vitamin D, calcium, zinc, and vitamin B-12. Much of this benefit is likely related to the low body weights, low blood pressure, and low blood cholesterol concentrations generally observed for vegetarians due to their lower intakes of saturated fats, cholesterol, and calories. Vegetarians are reported to have a lower risk of dying from ischemic heart disease⁵² and have a reduced all-cause mortality.⁵³

4.2.4. Okinawan Diet

Equally notable is the wide variation in other aspects of healthy diets such as macronutrient intake, represented most notably by the healthy Okinawan diet, which is low in fat and high in carbohydrates (mostly from vegetable sources). This suggests that low-energy, nutrient-dense diets with high-quality carbohydrates may be beneficial for reducing the risk of CVD among many chronic diseases.⁵⁴ The cardioprotective benefit of Okinawan diet is ascribed, in part, to the low consumption of saturated fat. Other possible mechanisms, such as the high contents of phytochemicals, high antioxidant intake, and low glycemic load in this diet, are also likely to be contributing to decreased risk for CVD and some cancers through multiple mechanisms, including reduced oxidative stress. A comparison of the nutrient profiles of the previous dietary patterns shows that the traditional Okinawan diet is the lowest in fat intake, particularly in terms of saturated fat, and highest in carbohydrate intake, in keeping with the very high intake of antioxidant-rich yet calorie-poor orangeyellow root vegetables, such

as sweet potatoes, and green leafy vegetables.⁵⁵ The longevity of Okinawan populations suggests that such a diet may even help to slow the aging process itself.⁵⁶

5. Some important nutraceuticals in the prevention of CVD

5.1. Arrhythmia

Fatty acids of the omega-3 series (n-3 fatty acids) present in fish are well established dietary components affecting plasma lipids and the major cardiovascular disorders, such as arrhythmias.^{57,58}

5.2. Atherosclerosis

Octacosanol is a 28-carbon chain alcohol. This nutraceutical is present in fruit, leaves and skin of many plants and whole grains.⁵⁹ Lipid lowering effects. Since it has no side effects further studies may be undertaken to prove the claims.⁶⁰ Bovine milk fat globule act as anticardiovascular disease, anticholesterolemic, coronary heart disease⁶¹

5.3. Coronary Artery Disease

Flavonoids are widely distributed in onion, endives, cruciferous vegetables, black grapes, red wine, grapefruits, apples, cherries and berries.⁶² Flavanoids in plants available as flavones (containing the flavonoid apigenin found in chamomile); flavanones (hesperidin - citrus fruits; silybin- milk thistle flavonols (tea: quercetin, kaempferol and rutin grapefruit; rutin buckwheat; ginkgo flavonglycosides - ginkgo),⁶³ play a major role in curing the cardiovascular diseases.^{64,65} Flavonoid intake was significantly inversely associated with mortality from coronary heart disease and the incidence of myocardial infarction. Flavonoids in regularly consumed foods may reduce the risk of death from coronary heart disease in elderly men.⁶⁶

5.4. Hypertension and lipid lowering

Optimal nutrition, nutraceuticals, vitamins, antioxidants, minerals, weight reduction, exercise, cessation of smoking, restriction of alcohol and caffeine plus other lifestyle modifications can prevent, delay the onset, reduce these verity, treat, and control hypertension. Nutrients and nutraceuticals with calcium channel blocking activity (thus antihypertensive activity) include α -Lipoic acid, magnesium, Vitamin B6 (pyridoxine), Vitamin C, Nacetyl cysteine, Hawthorne, Celery, ω -3 fatty acids etc.⁶⁷ Animal studies provide provides

sound mechanistic basis for the use of ginger in hypertension and palpitations.⁶⁸ Nutritional value of egg is increased because of added gamma linolenic acid (GLA) which has many benefits, including prevention and management of CVD like hypertension.⁶⁹ The relationship between dietary factors and CVD has been a major focus of health research for almost half a century. Epidemiological and clinical studies indicate that the risk of CVD is reduced by a diet rich in fruits, vegetables, unrefined grains, fish and low-fat dairy products, and low in saturated fats and sodium.⁷⁰ Other foods such as mono and polyunsaturated fats, brans, nuts, plant sterols, and soy proteins have all been shown to have a favorable effect on lipid profile and blood pressure.^{71, 72}

5.5. OBESITY

Cholesterol has long been implicated as a significant risk factor in cardiovascular disease. Sterols occur in most plant species and are called as phytosterols. Although green and yellow vegetables contain significant amounts, their seeds concentrate the sterols. Phytosterols compete with dietary cholesterol by blocking the uptake as well as facilitating its excretion from the body. Phytosterols in diet have the potential to reduce the morbidity and mortality from cardiovascular disease.⁷³ Fagopyrum esculentum Moench (common buckwheat or sweet buckwheat), originated in Asia. Buckwheat seeds possess proteins, flavonoids, flavones, phytosterols, thiamin-binding proteins etc. Buckwheat proteins are beneficial in constipation and obesity and more importantly lower cholesterol and high blood pressure.⁷⁴

CONCLUSION

Nutraceuticals have received considerable interest because of their presumed safety and potential nutritional and therapeutic effects. Major cardioprotective bioactive foods and nutraceuticals are now part of nutrition supplements at nonprescription counters and their self-prescription is increased at large scale. Diet is also very important to prevent cardiovascular diseases. The biochemical mechanisms of nutraceutical action in cardioprotection are poorly reported. However, still cardiovascular disease remains a major threat because of high mortality compounded with incomplete success of chemotherapy and surgery intervention. In future, bioengineered nutraceuticals will play significant role in CVD prevention as alternative therapeutics.

Increasing evidence that health is related to diet have resulted in a range of government initiatives designed to encourage healthy eating, and positive steps are being taken by an increasing number of individuals. The perception that conventional medicines cannot successfully treat all diseases and that many modern pharmaceuticals are ineffective in certain disease states and have marked side effects has led many people to look to the nutraceuticals for alternative therapies. So it is very important to clarify the process for documenting the health benefits of nutraceuticals, increase research funding for both basic and applied studies related to nutraceuticals, and to improve communication of nutraceutical benefits and risks to common peoples.

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